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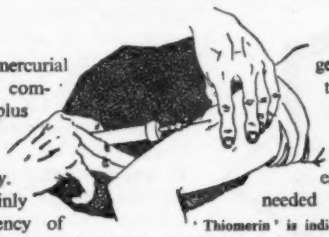

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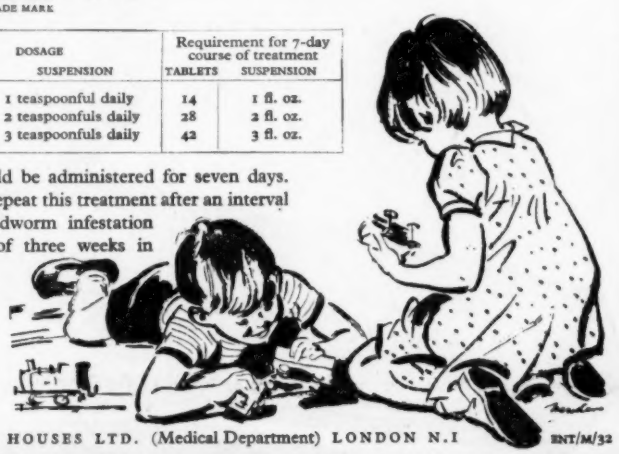

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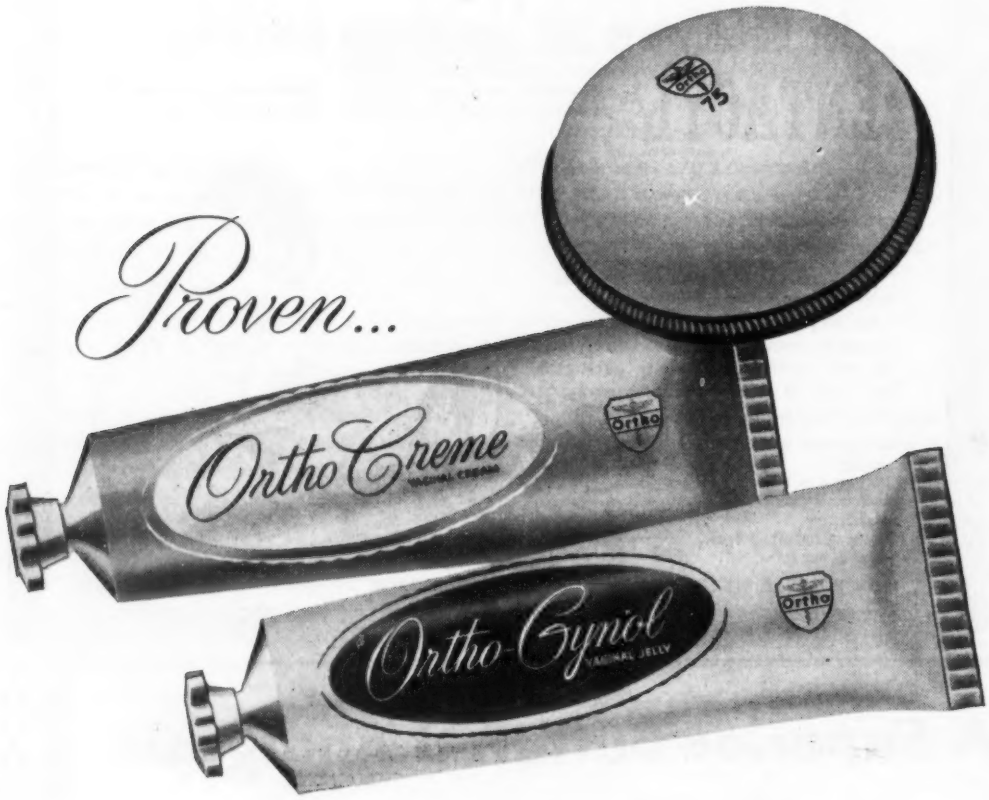

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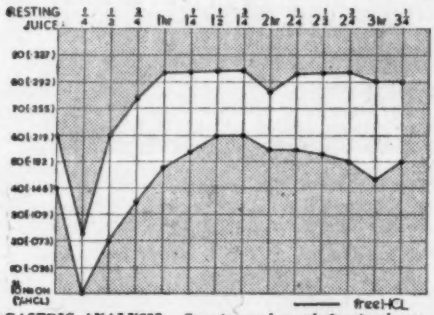
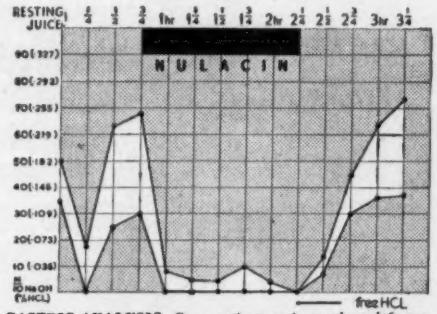
Nulacin tablets are not advertised to the public, have no B.P. equivalent, and may be prescribed on E.C.10. The dispensing pack of 25 tablets is free of Purchase Tax. (Price to Pharmacists is 2/-.) Also available in tubes of 12.

Nulacin is available throughout the British Commonwealth, in the U.S.A. and in many other countries. It is known as Nulactin in Canada and Sweden.



GASTRIC ANALYSIS. *Superimposed gruel fractional test-meal curves of five cases of duodenal ulcer.*



GASTRIC ANALYSIS. *Same patients as in graph on left, two days later, showing the striking neutralizing effect of sucking Nulacin tablets (3 an hour). Note the return of acidity when Nulacin is discontinued.*

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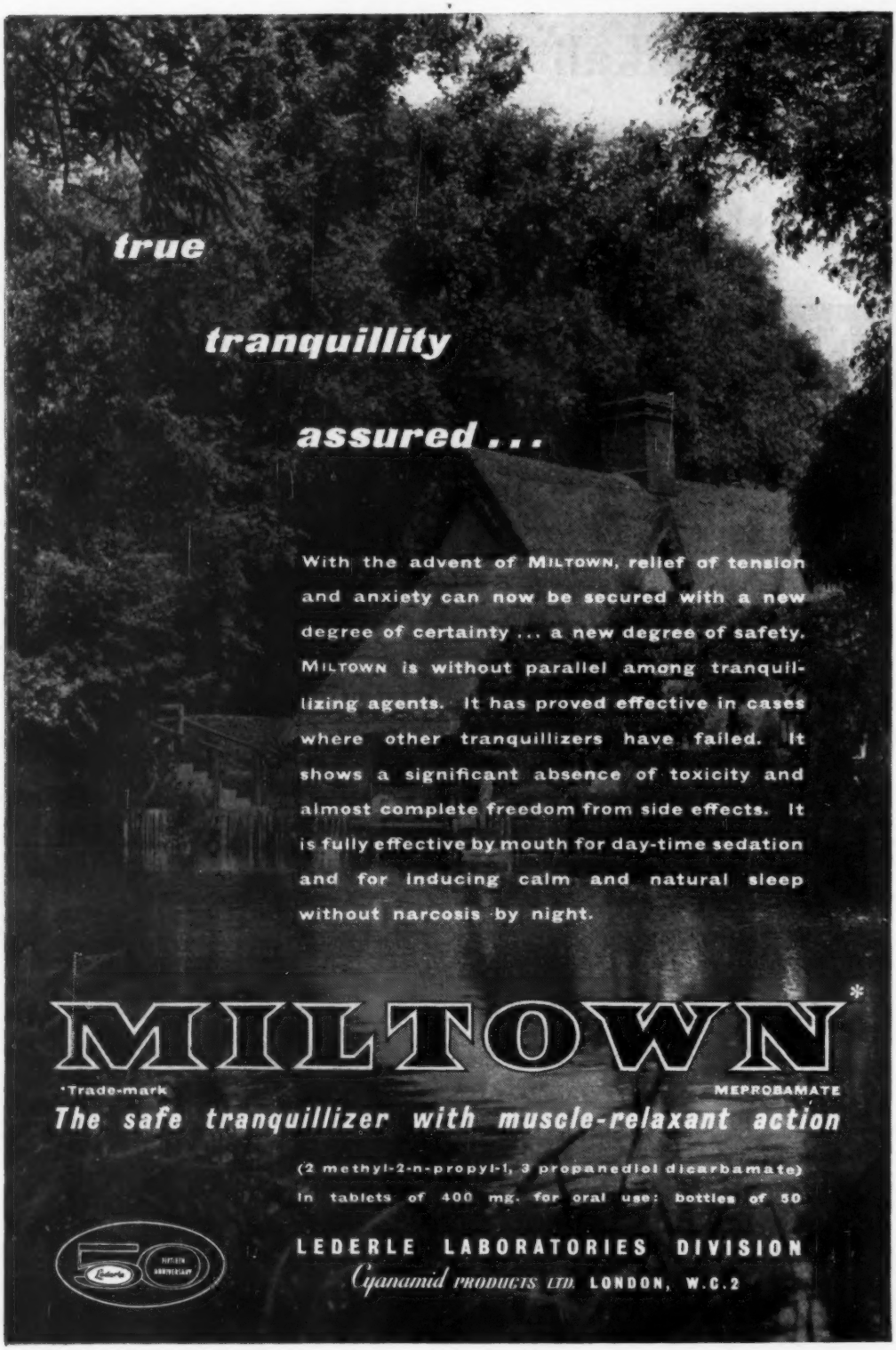
The Control of Gastric Acidity. *Brit. Med. J.* 26th July, 1952, **2**: 180-182. Medical Treatment of Peptic Ulcer. *Med Press* 27th February, 1952, **227**: 195-199. Notes on Remedial Agents. *Med Rev.* September, 1952, **46**: 162. Discussion on Peptic Ulceration. *Proc. Roy. Soc. Med.* May 1953, **46**: 354. The Effect on Gastric Acidity of "Nulacin" tablets. *Med. J. Aust.* 28th November, 1953, **2**: 823-824. Control of Gastric Acidity by a New Way of Antacid Administration. *J. Lab. Clin. Med.* 1953, **42**: 955. Further Studies on the Reduction of Gastric Acidity. *Brit. Med. J.* 23rd January, 1954, **1**: 183-184. Clinical Investigation into the Action of Antacids. *The Practitioner* July, 1954, **173**: 46. Management of Peptic Ulceration in General Practice. *Med. World* December, 1954, **81**: 591-601. Ambulatory continuous Drip Method in the Treatment of Peptic Ulcer. *Amer. J. Dig. Dis.* March, 1955, **22**: 67-71. Notes on Remedial Agents. *Med. Rev.* October, 1955, **49**: 142. Antacids in Peptic Ulcer. *The Practitioner*, January, 1956, **176**: 103.

Samples available on request

HORLICKS LIMITED

Pharmaceutical Division, Slough, Bucks.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The safe tranquillizer with muscle-relaxant action
(2 methyl-2-n-propyl-1, 3 propanediol dicarbamate)
In tablets of 400 mg. for oral use: bottles of 50
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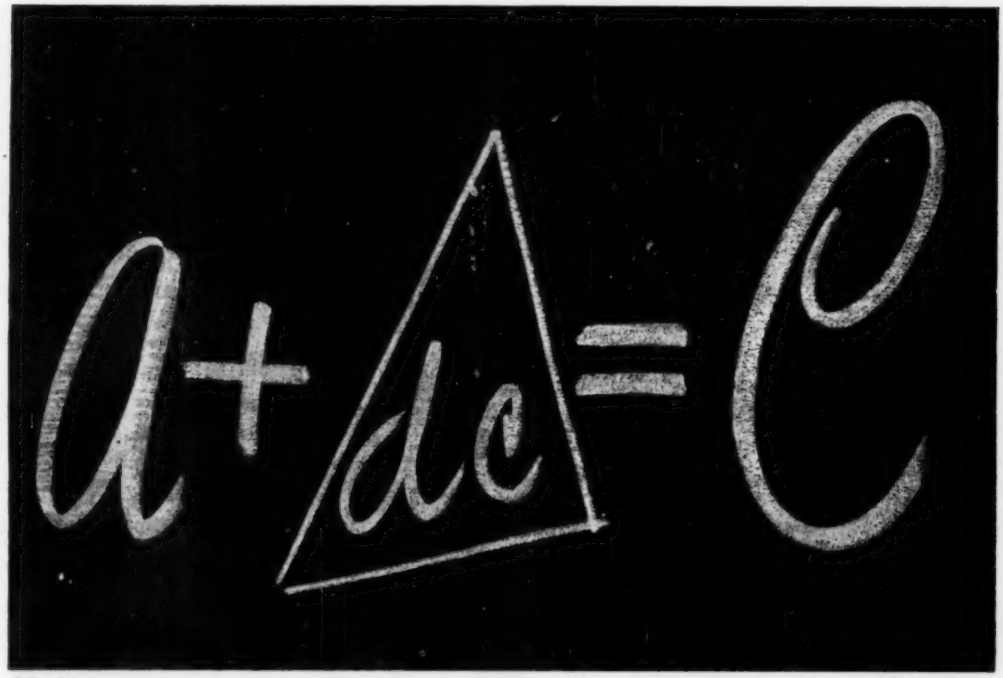

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additive anti-inflammatory effects

decreased side-effects

In rheumatic disease Aspirin + Delta-Cortef* (PREDNISOLONE) = **Cordex**

Cordex combines Delta-Cortef and acetylsalicylic acid to provide the additive *anti-inflammatory* activity of each drug, plus the *analgesic* action of the salicylate. With this combination relief of pain is normally afforded in 24 to 72 hours. In the amount employed, Cordex achieves an effect equal to that produced by 2 or more times the amount of adrenal steroid alone. This combination permits a reduction in the dosage of each component, which results in a decrease in undesired side reactions.

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Each CORDEX tablet contains:

Delta-1-hydrocortisone (Prednisolone) .....0.5 mg.

Acetylsalicylic acid .....300.0 mg.

Average dosage 1-2 tablets four times a day.

Bottles of 100 tablets.

CORDEX is at present available to hospitals only. *Trade mark

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13

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HYALASE greatly enhances the spread and absorption of the anaesthetic. It can be easily combined with the local anaesthetic with or without adrenaline, producing a greater area of anaesthesia of satisfactory duration.

HYALASE can be successfully applied whenever infiltration anaesthesia is the method of choice.

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Primarily intended for the 3-10 age-group, Paladac is equally suitable for adolescents and adults where liquid medication may be preferred.

Paladac is supplied in bottles of 4 and 16 fl. ozs.

Each teaspoonful (4 c.c.) contains:— Vitamin A 5,000 units, Vitamin D 1,000 units, Vitamin B_1 (Aneurine Hydrochloride) 3 mg., Vitamin B_2 (Riboflavin) 3 mg., Vitamin B_6 (Pyridoxine Hydrochloride) 1 mg., Nicotinamide 20 mg., Vitamin C (Ascorbic Acid) 50 mg.

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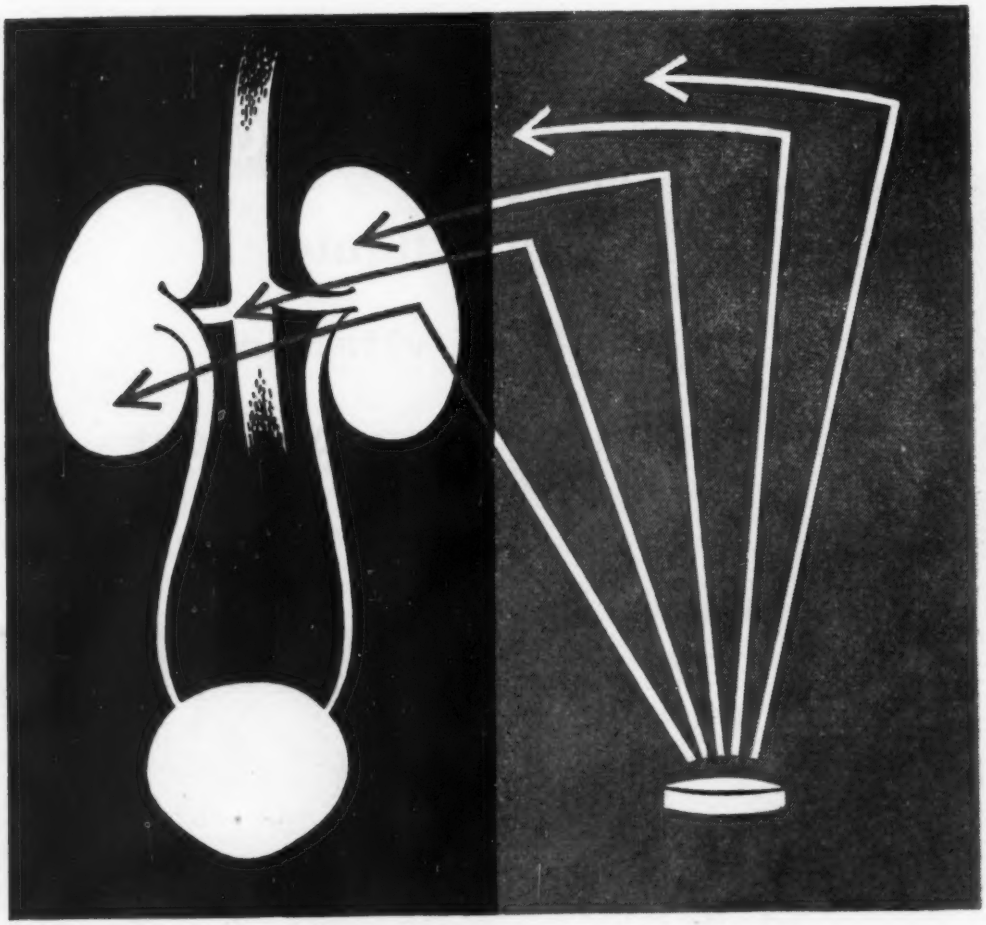

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The high solubility and low acetylation of Urolucosil mean that it is rapidly excreted into the urinary tract without risk of crystalluria. As a result, high urine concentrations can be quickly attained.

That is why Urolucosil is so effective against B. coli infections of the urinary tract. Small doses are highly effective, and side-effects are rare. The maintenance dose of Urolucosil can be continued for many months without risk of toxic reactions.

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Sulphamethizole 0.1G.

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1 tablet 4-hourly.

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In bottles of 25, 250 and 1,000 tablets.

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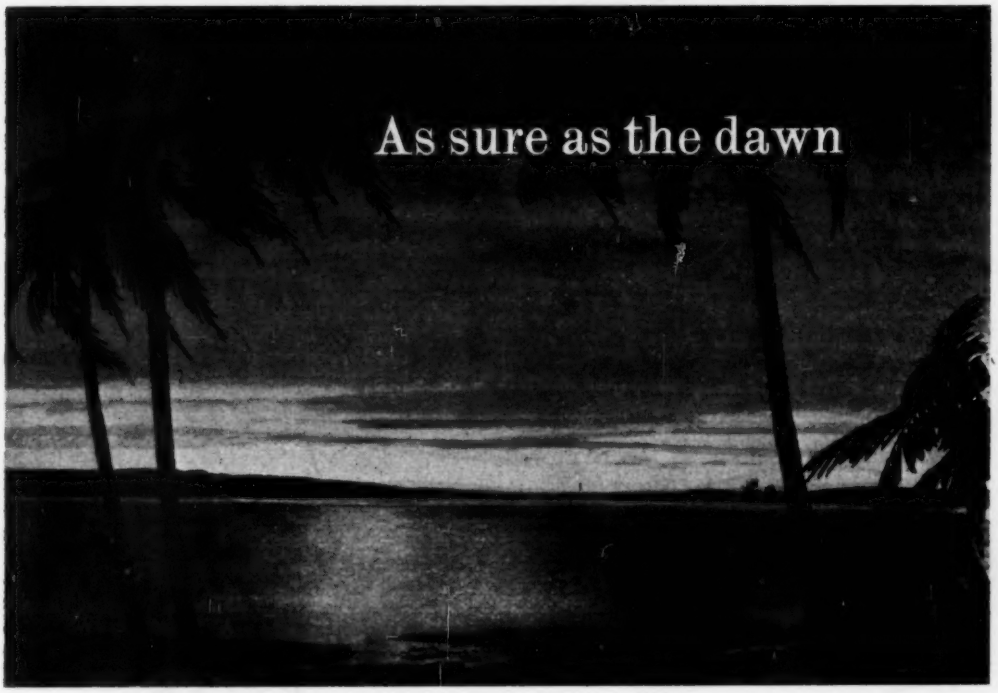

On injecting Cytamen—crystalline vitamin B_{12}—a doctor can be as confident of that injection as he is in the certainty of dawn. Confident that each dose is an exact weight of crystalline vitamin B_{12} . . . that the stated potency cannot vary . . . that varied response on the part of the patient therefore is not and cannot be due to the product . . . that he has at his command a range of potencies which allows complete flexibility of treatment. In short, Cytamen puts into the doctor's hand the most therapeutically efficient and the most economical means of combating pernicious and other macrocytic anaemias.

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Crystalline vitamin B_{12}

50, 100, 250 *and* 1,000 *micrograms per cc.*

In India and Switzerland Cytamen is known as 'Macrabin'

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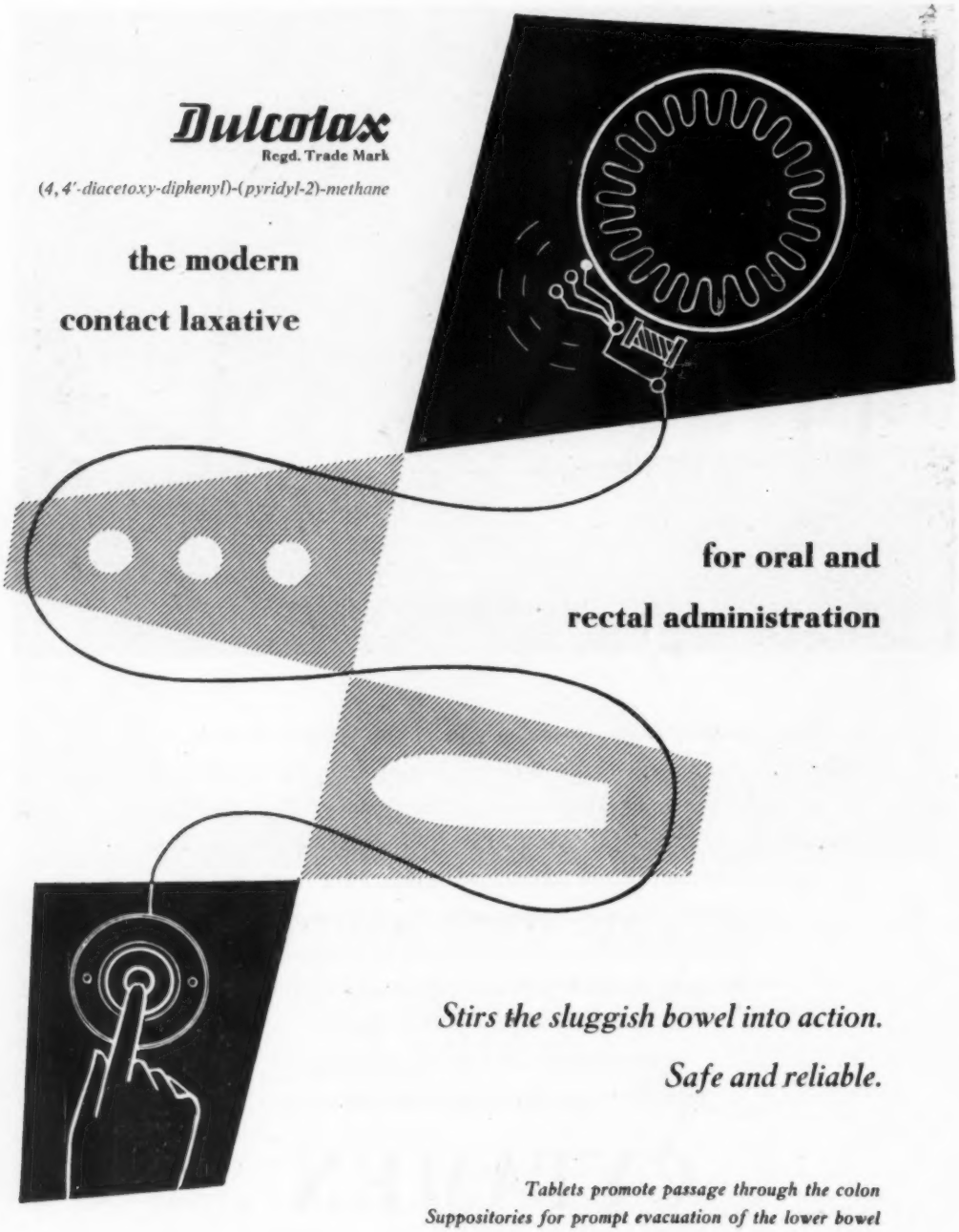

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Stirs the sluggish bowel into action.

Safe and reliable.

Tablets promote passage through the colon
Suppositories for prompt evacuation of the lower bowel

Dulcolax enteric coated tablets of 0.005 g. · Bottles of 30 and 200
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A NEW FAT-STORED ŒSTROGEN

TACE

may change present-day concepts of œstrogen therapy because:—

TACE is stored in body fat—its activity is gradually released in a manner closely resembling natural œstrogen secretion.

TACE is free from side effects. Nausea, vomiting and œstrogen withdrawal bleeding in the female and painful gynæcomastia in the male are not produced.

TACE has virtually no effect on the pituitary gland. Resistance does not develop on prolonged therapy—'TACE' is therefore of particular value in the treatment of prostatic carcinoma where it will often continue to control the condition when resistance to other œstrogens has developed.

INDICATIONS

1. MENOPAUSAL SYNDROME
2. INHIBITION OF LACTATION
3. PROSTATIC CARCINOMA

REFERENCES

The Storage of Estrogen in Human Fat after Estrogen Administration. Amer. J. of Obstetrics & Gynecology (1952) **63**:1361.

A Fat-Soluble Estrogen—Use in the Treatment of Menopausal Distress. Amer. J. of Obstetrics & Gynecology (1954) **2**:201.

Preliminary Experience in Treatment of the Menopause with Tace, a new Type of Estrogen. Journal of Clinical Endocrinology and Metabolism (1954) **14**:272.

Management of the Menopause. Editorial, J. Amer. med. Ass. (1955) **158**:566.

Merrell

'TACE' is available in capsules each containing 12 mg. chlorotrianisene in bottles of 60 and 300 capsules.

Detailed literature is available on request.

'TACE' brand chlorotrianisene is distributed in the United Kingdom and Eire by

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Pacatal

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9-(1-methyl-3-piperidylmethyl) phenothiazine.

a powerful yet safe tranquillizing drug

Clinical trials in many countries have proved PACATAL to be highly effective in mental disturbances ranging from the psychoneuroses to the psychoses.

PACATAL reduces tension, makes the patient quieter, less confused—but still alert, objective, co-operative, amenable to psychotherapy.

NOW available in ampoules for parenteral administration.

In anaesthetic medication, PACATAL reduces tension and anxiety in the pre-operative period, provides smooth and safer induction and potentiates anaesthetics. Post-operatively PACATAL aids rapid recovery and reduces nausea and vomiting.

PACATAL can be administered with complete confidence, being of low toxicity and uniquely free from troublesome side-effects.
It is rapidly absorbed and quickly eliminated, thus ensuring against cumulative dangers.

Pacatal **is available in tablets for oral administration and ampoules for parenteral use.**

***Tablets** 25 mg. in bottles of 50 and 500.*
***Ampoules** 2 ml., 25 mg./ml. in boxes of 10 and 50.*

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the new one-dose post-operative analgesic

PROLADONE

Dihydrohydroxycodeinone pectinate

Clinical trials have shown that, in most cases, satisfactory post-operative pain control is obtained with one injection.

DOSE: *1 ml by intramuscular injection.*
PACKING: *1 ml. ampoules in boxes of six.*
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THE CROOKES LABORATORIES LIMITED · PARK ROYAL · LONDON · N.W.10

in senile pruritus vulvae...

KOLPON

Pessaries (IMPROVED FORMULA)

When the problem is the rehabilitation of the hypo-oestrogenic vagina, Oestrone, in the form of Kolpon Pessaries, will be found to be uniformly and strikingly effective.

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One pessary each night or on alternate nights while symptoms persist.

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Pessaries containing 0.1 mg. or 1.0 mg. oestrone in water soluble wax base in boxes of 5 or 25.

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For infections of the mouth and throat and for the relief of sore throat and laryngitis

'HIBITANE'

antiseptic lozenges

Containing the new I.C.I. antiseptic 'Hibitane' (Chlorhexidine)
Formula: 'Hibitane' Dihydrochloride 5 mg. Benzocaine B.P. 2 mg.

ADVANTAGES

1 Powerful antibacterial effect against Gram-positive and Gram-negative organisms. Also active against Monilia and Aspergillus.

2 The saliva produced when sucking a lozenge is highly bactericidal to mouth pathogens. Saliva tests show 'Hibitane' lozenges to be far superior to other antiseptic lozenges.

3 Low oral toxicity; harmless to the tissues locally.

4 No sensitivity reactions, local or general, have been reported with 'Hibitane'.

5 Bacteria do not develop resistance to 'Hibitane', nor can resistance be induced *in vitro*.

6 The lozenges are pleasantly flavoured and well liked by children.

HIBITANE

'Hibitane' Lozenges are issued in tubes of 12. Basic N.H.S. cost: 1/5d. (plus purchase tax) for 12 lozenges.

IMPERIAL CHEMICAL (PHARMACEUTICALS) LIMITED, WILMSLOW, CHESHIRE
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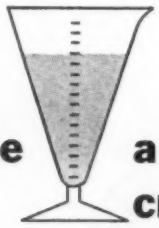

Take a conventional analgesic cream formula and add

① **a powerful vasodilator** (*Perdilatal*)

② **a superior analgesic** (*Propyl salicylamide*)

and you have

thermona

TRADE MARK

A new development for the relief of pain in the group of conditions covered by the terms 'muscular rheumatism' or 'fibrositis'.

The vasodilator PERDILATAL (1-(p-hydroxyphenyl)-2-(l'methyl-3'-phenyl-propylamino)-propanol-(1) hydrochloride): a highly vaso-active substance formerly known as Dilatal which, when given systemically, produces an increase in both muscle circulation (1) and cardiac output (2) and gives rise to a prolonged hyperaemia of the deep tissues.
The analgesic PROPYL SALICYLAMIDE: an analgesic more powerful than other derivatives of salicylamide and salicylic acid (3).

Methyl nicotinate, a superficial rubefacient, facilitates the absorption of the other active substances through the skin and reinforces the effect of Perdilatal. Similarly glycol salicylate adds to the analgesic effect of propyl salicylamide.

THERMONA contains the following ingredients: 0.3% Perdilatal, 1.0% methyl nicotinate, 5.0% propyl salicylamide, 10.0% glycol salicylate, 83.7% vanishing cream base.
THERMONA is available in tubes containing 20.G. (approx.). It is prescribable on N.H.S. form E.C.10.

references

1 *Z. KreislForsch.* 1954, 43, 756
2 *Angiology* 1954, 5, 314
3 *J. Pharmacy & Pharmacol.* 1952, 4, 872

S&N *Further information from Smith & Nephew Ltd., Welwyn Garden City, Herts.*

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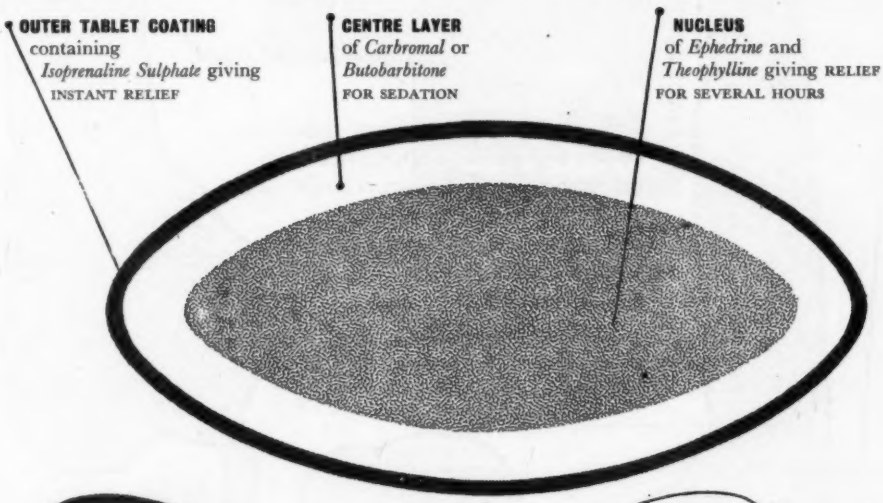
SUSTAINED RELIEF OF BRONCHIAL ASTHMA

PROVIDED BY RELAY ACTION IN A SINGLE TABLET



BY NIGHT

FYDAL

FYDAL TABLETS, containing Butobarbitone, are intended for night use and should be taken when premonitory symptoms of an attack appear.

Formula: Ephed. Hydrochlor., B.P. 32 mg.
Theophyll., B.P. 64 mg.
Isoprenal. Sulph., B.P. 10 mg.
Butobarbitone, B.P.C. 48 mg.

Basic N.H.S. price . . . . foil-pack of 10 tablets . . . 1/8d.

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FYDALEX

FYDALEX TABLETS, contain Carbromal in place of Butobarbitone and are for use during the day. Like FYDAL, they provide immediate and prolonged relief.

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Carbrom., B.P.C. 96 mg.

Basic N.H.S. price . . . . foil-pack of 10 tablets . . . 1/4½ & 5d. P. Tax

Used conjointly, FYDAL and FYDALEX provide an effective round-the-clock treatment and may be prescribed accordingly.

Literature and further information available from

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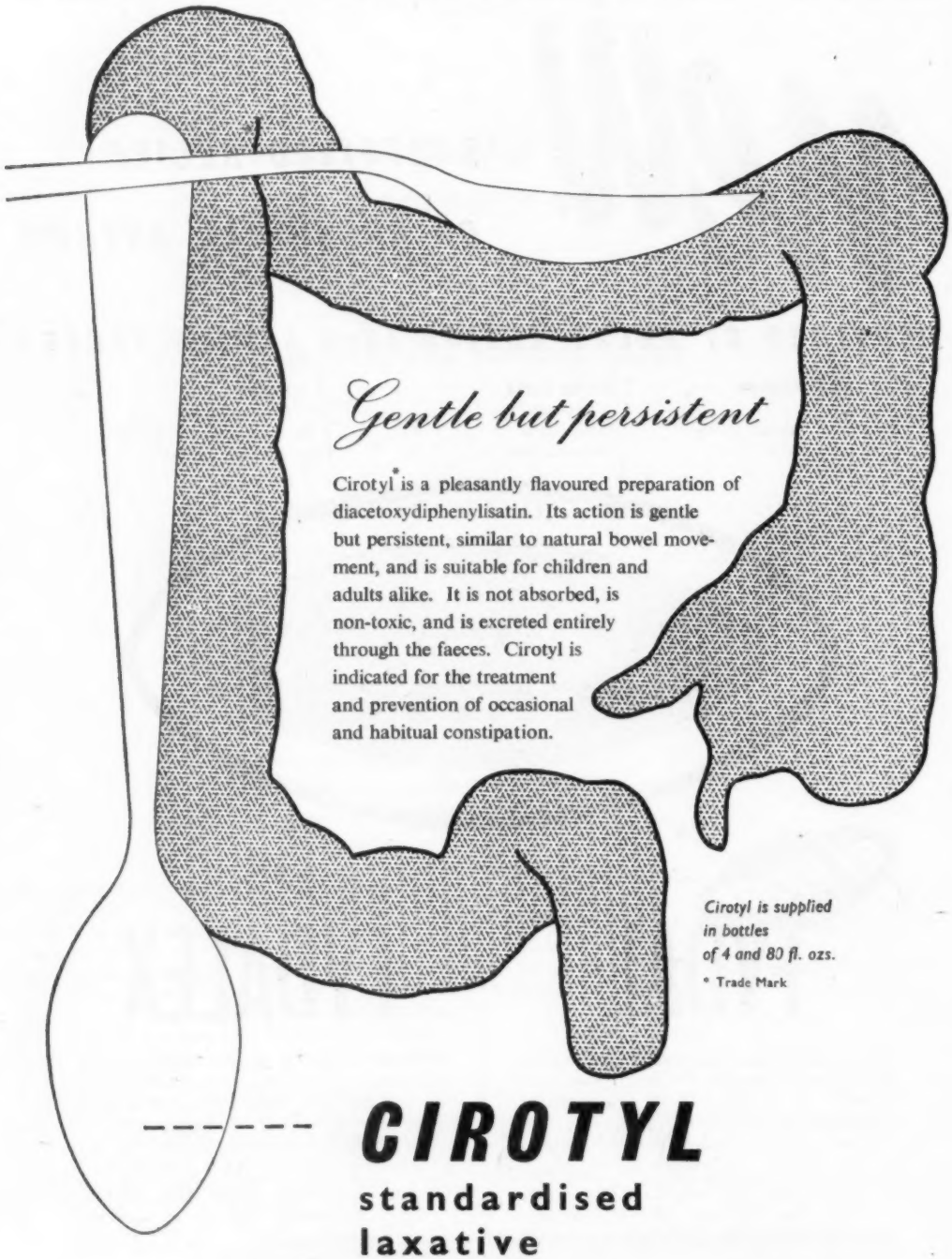

Gentle but persistent

Cirotyl* is a pleasantly flavoured preparation of diacetoxydiphenylisatin. Its action is gentle but persistent, similar to natural bowel movement, and is suitable for children and adults alike. It is not absorbed, is non-toxic, and is excreted entirely through the faeces. Cirotyl is indicated for the treatment and prevention of occasional and habitual constipation.

Cirotyl is supplied in bottles of 4 and 80 fl. ozs.

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CIROTYL

standardised laxative preparation

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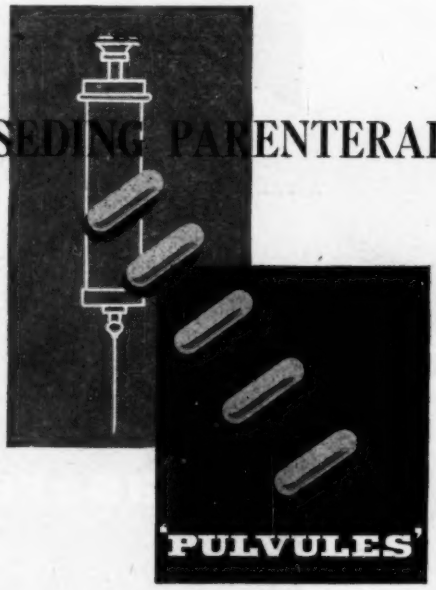

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THE *effective* **ORAL PENICILLIN**

Reports prove that Penicillin-V will give clinical results comparable with parenteral penicillin. The oral route is time-saving and painless. Blood levels are higher and more prolonged than with other oral penicillins. Penicillin-V is unique in that it is unaffected by the action of gastric acid. Whenever penicillin is indicated, Penicillin-V is the product of choice.

The average dose is one 125 mg. capsule four times daily increased in severe infections.

'Pulvules' Penicillin-V Lilly each contains 125 mg. (200,000 units). Suspension Penicillin-V Lilly Paediatric, in bottles to make 60 cc. contains 62.5 mg. (100,000 units) per large teaspoonful.

Lilly TRADE MARK

ELI LILLY & COMPANY LIMITED

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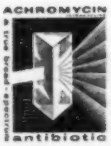
ACHROMYCIN*
TETRACYCLINE

drop by drop

Administration of small doses of ACHROMYCIN tetracycline is considerably simplified by the introduction of a new improved presentation of the antibiotic—ACHROMYCIN Liquid Pediatric Drops, which is issued in a small pliable plastic bottle with dropper nozzle. The bottle is designed to deliver 5 mg. of ACHROMYCIN in each drop. ACHROMYCIN Liquid Pediatric Drops is a pleasant cherry-flavoured preparation intended particularly for infants and children where palatability is a factor. The dose from the dropper bottle can be conveniently added to milk, water or fruit juices.

ACHROMYCIN* LIQUID PEDIATRIC DROPS
TETRACYCLINE

Ready to use—an improvement on the earlier form of ACHROMYCIN Pediatric Drops (requiring suspension in water) which it now replaces. *Available in 10 cc. dropper bottles—100 mg./cc.* * REGD. TRADE MARK



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Cyanamid PRODUCTS LTD. LONDON, W.C.2.

In anxiety states . . . . . three-fold effective therapy

Anxine Tablets provide the complete symptomatic treatment of anxiety states by improving mood and increasing confidence, by inducing gentle sedation and allaying anxiety, and by securing the optimal degree of muscular relaxation.

Although each of the three components of Anxine Tablets, dexamphetamine sulphate, cyclobarbitone and mephenesin, makes an important contribution to the amelioration of the symptoms of anxiety states, none is adequate alone. It is only when they are combined, in the form of Anxine Tablets, that maximum control of symptoms is achieved.

Anxine Tablets are indicated in the treatment of anxiety states, psychoneuroses and psychosomatic disorders. Anxine will produce rapid improvement in cases where mental or emotional tension is an important factor, in depression and neurasthenia, and in those patients suffering from the many ill-defined anxieties and fears which can so profoundly and adversely affect general health.

ANXINE

Each tablet contains :—

DEXAMPHETAMINE SULPHATE	2·5 mg.
CYCLOBARBITONE	35 mg.
MEPHENESIN	120 mg.

C56/160/161H

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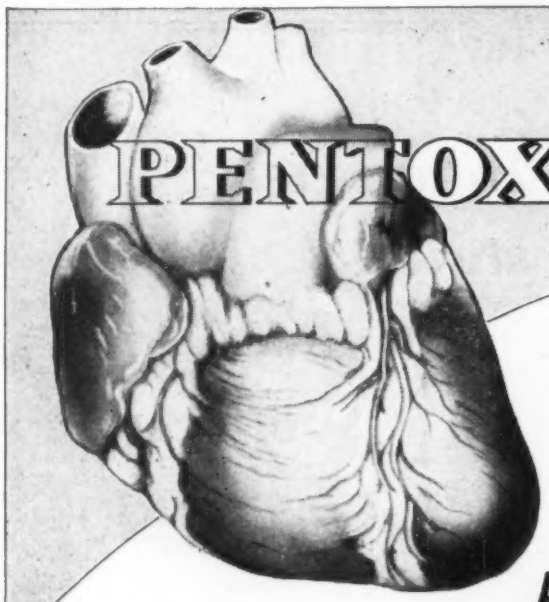

PENTOXYLON

... the new therapy for Angina Pectoris

In 'Pentoxylon' the tranquillizing, bradycardic influence of 'Rauwiloid' brand alkaloid hydrochlorides of Rauwolfia serpentina is allied to the prolonged vasodilating effect of pentaerythrityl tetranitrate. This new combined therapy represents an important advance in the long term treatment of angina pectoris.

Although some patients will still occasionally require glyceryl trinitrate, in many others 'Pentoxylon' will provide complete relief from anginal attacks. It will also bring: "*gratifying reduction of anxiety and relief of apprehension . . .*"

North-West Med. (1955) 54: 34

Dose: 1 tablet four times a day, before meals, increased later if necessary.

RIKER

'Pentoxylon' is available in tablets, each containing 1 mg. of 'Rauwiloid' and 10 mg. of pentaerythrityl tetranitrate, available in bottles of 25, 100 and 500.

'RAUWILOID' and 'PENTOXYLON' are registered trademarks
Registered Users:

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Introducing 'migril' for

3D relief in migraine

Dispels headache
Disperses visual disturbances
Defeats nausea and vomiting

A new product—'Migril'—provides, for the first time, a successful 3-way attack on migraine.
'Migril' contains ergotamine tartrate (2 mgm.), caffeine (100 mgm.) and cyclizine hydrochloride (50 mgm.) in each tablet. The inclusion of cyclizine hydrochloride not only eliminates the nausea and vomiting often associated with migraine but also **enables larger and more effective doses of ergotamine to be administered.**

'migril' BRAND

Ergotamine Compound *(Compressed)*
PACKS OF 10 AND 100

BURROUGHS WELLCOME & CO. (THE WELLCOME FOUNDATION LTD.) LONDON

Is it going to hurt?

There are many wounds of all types which require dressing in such a way that the delicate epithelium receives the minimum of trauma. Most burns and many of the lesser accidents to which children are subject come into this category.

In such cases, consider the advantages of Jelonet paraffin gauze dressing. This non-adherent dressing, a Smith & Nephew product, comes to you sterilized for immediate use in your surgery. It need exert no more pressure over the damaged part than is absolutely necessary; dressing trauma is prevented, and healing can continue undisturbed.

Jelonet dressings are supplied in tins and in separately-packed single pieces, in sealed envelopes, for use in the patient's home.

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CLINICAL TESTS OF THYROID FUNCTION *

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CLINICAL tests are invented to help us reach diagnoses not obvious on clinical examination alone. Many patients with disorder of the thyroid gland present obvious clinical signs and do not need tests. For the others several tests of total function of the thyroid gland can be applied, but here we are only concerned with the three main tests, each of which assesses a separate aspect of thyroid function. They have different limitations and different fields of usefulness and so can supplement the usefulness of each other.

I shall try to assess both the comparative usefulness of the three main tests of total thyroid function—the basal metabolic rate (B.M.R.) and estimations of radio-iodine and of the level of protein-bound iodine in the plasma—and, in particular, their sources of error and their application in the less obvious disorders.

(1) The longest-established test is the estimation of the B.M.R. from the basal consumption of oxygen. This assesses the general effect of the thyroid hormone on the body tissues and gives the best index of the severity of thyroid dysfunction.

(2) The radio-iodine test in any of its various forms measures the activity of the cells of the thyroid gland by assessing the speed of movement of iodine through the body. This test gives a reliable reflection of thyroid-cell activity if the intake and stores of iodine are normal. Combined tests, and radio-iodine tests after standard drug loads, can be used when unexpected results suggest the presence of abnormal stores of iodine.

(3) The plasma level of protein-bound iodine can be estimated chemically, but only with difficulty because of the small amounts involved. This nearly always gives a good index of the level of circulating thyroid hormone, except after the administration of drugs containing organic iodine (Salter et al. 1949, Starr et al. 1950, Hallman et al. 1951, De Mowbray and Tickner 1952, Riggs 1952); but this test can be reliable only in meticulously careful laboratories. Proper use of the other two tests makes it unnecessary for most clinical problems; it can provide a useful supplement to the other two tests, both for occasional unusual problems, and for improving the radio-iodine test.

Patients Tested

At Hammersmith Hospital we have now had more than five years' experience of all three main tests of thyroid function, having applied them several thousands of times each. The following arguments are based on this experience and almost exclusively on patients whom I have also examined clinically.

Only tests made before July, 1955, were analysed. Hence in all cases a final clinical diagnosis could be made in the light of at least three months' response to appropriate treatment. Where there was no clear therapeutic response, normal thyroid function was inferred. Though some minor deviations may thus have been missed, it is only the treatable thyroid disorder that the clinician wishes to select.

During the past five years the data were analysed on different occasions; each analysis included all the patients tested during the chosen period except some (up to 2%) excluded because of either verified test errors or unclear final diagnosis. In each analysis the patients recently treated with either drugs or thyroid gland were separated, so that the influence of such treatment on the tests might be considered.

Group A consisted of the first 100 patients tested in 1953 simultaneously by three or more radio-iodine procedures.

Group B consisted of the 112 patients whose B.M.R. was estimated during sleep in 1952–54—i.e., most of those admitted then for assessment of thyroid function.

Group C consisted of those tested by at least two, and usually all three, main tests of thyroid function from 1953 to the first half of 1955: 162 patients, including 71 with proved thyrotoxicosis or myxœdema and 52 tested after various drugs or thyroid treatments. Such triple testing (B.M.R., radio-iodine, and level of protein-bound ^{127}I in the plasma) was done at first on some typical cases to provide a basis for comparison and later only in diagnostic problems.

Group D consisted of 72 patients retested with ^{131}I after a standard load of iodide, a special test used to distinguish iodide deficiency from hyperthyroidism.

Group E comprised 31 patients tested with radio-iodine after stimulation by thyroid-stimulating hormone.

Relative Sensitivity to Thyroid Dysfunction

It will be useful to compare first the relative sensitivity of these three main tests to increased and to decreased thyroid function. Fig. 1 compares the separation from the normal range made by these three tests on groups of proved thyrotoxic and myxœdematous patients given all three tests simultaneously.

Segregation by severity is done best by the B.M.R., but there is some overlap into the normal range by both abnormal groups.

The radio-iodine test segregates the thyrotoxic group well away from the normal range, though some non-toxic goitres show similarly high uptakes by any test (Pochin 1950, Wayne 1954). Severe or complete myxœdema is also fully distinguished on all three tests; but mild myxœdema overlaps the normal range even more on the radio-iodine test than on either of the others.

The chemical estimation of protein-bound ^{127}I in the plasma distinguishes most, though not all, thyrotoxics but stands out best of the three tests for its separation of myxœdema, mild as well as severe. The 3 mild myxœdema cases shown overlapping into the normal range gave dubiously abnormal values of 3·2, 3·2, and 2·8 μg. per 100 ml., all below our lowest normal value of 3·4 μg.

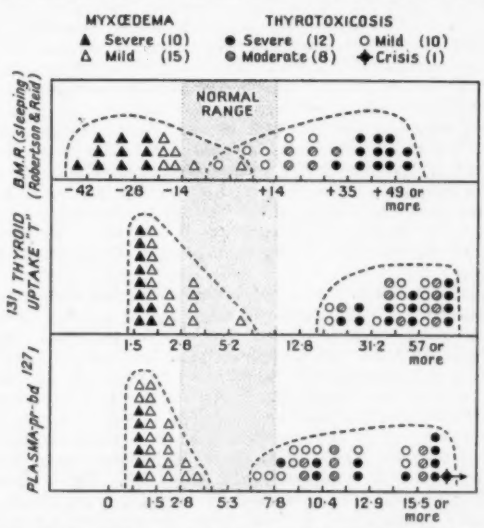


Fig. 1—Results of three main tests in proved myxœdema and thyrotoxicosis.

Patients are those of group C with proved thyrotoxicosis or myxœdema. Each scale is matched in standard-deviation ranges of normals in order to compare tests' sensitivities. Nearly all B.M.R.s were recorded sleeping, and their results are shown as percentage of appropriate mean Robertson and Reid (1952) standards. See fig. 3 for derivation of urinary T index of thyroid uptake.

* 8th Alex Simpson-Smith memorial lecture of the West London Hospital Medical School given on Oct. 25, 1955.

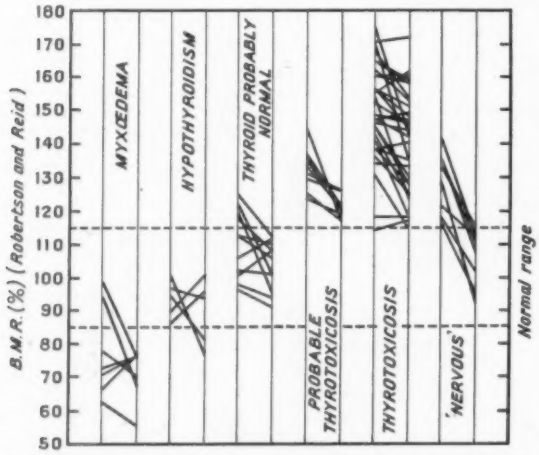


Fig. 2—Effect on B.M.R. of intravenous pentobarbitone sodium which induced sleep.

Clinical subgroups are those of patients of group B tested after intravenous sedation. Left-hand point represents lowest value of 2 or more B.M.R.s from patient awake, and right-hand point B.M.R. during sleep. Each result is expressed as percentage of appropriate Robertson and Reid (1952) standard. (From Fraser and Nordin 1955.)

per 100 ml. This test is probably most useful for confirming mild myxœdema when the other tests are normal, and for confirming suspected deficiencies of iodine.

Tests Considered Individually

ESTIMATION OF B.M.R.

The main limitation of this test—the difficulty of consistently achieving the basal state, particularly with nervous patients—may be overcome by preparatory sedation, after which the B.M.R. is estimated with the patient sleeping (Bartels 1949, Rapport et al. 1951, Fraser and Nordin 1955). The risks of anæsthesia can be avoided by using either intravenously a slower-acting barbiturate—e.g., pentobarbitone sodium—or orally three separate hourly doses of amylobarbitone sodium. But, for certainty about the basal state, the estimation should be made with the patient sleeping. The only real disadvantage of the sleeping or sedated B.M.R. is the subsequent drowsiness of the patient for the rest of the day; and this can now be overcome by the subsequent use of an oral barbiturate antagonist (Ibbertson et al. 1956).

When a B.M.R. has been estimated during sleep, it is important to use standards referable to a truly basal state—e.g., those of Robertson and Reid (1952). For these standards, but not the others, the healthy people were first given practice runs until two readings agreeing within 5% were obtained. When the result is expressed as a percentage of the mean normal of these standards, the value will be about 10% higher than when the older standards are used, and these Robertson and Reid standards show a normal range of ±14%. Fig. 2 shows how lower values are obtained by measuring the sleeping B.M.R., particularly in the case of nervous patients proved by other means to have no thyroid disease. Most of the B.M.R. values recorded in fig. 1 were measured with the patient sleeping.

RADIO-IODINE TESTS

These tests of thyroid function are now widely practised and useful clinical tests (Marinelli et al. 1948, Skanse 1949, Werner et al. 1949, Foote and Maclagan 1951, Foote et al. 1952, Fraser et al. 1953). We need not concern ourselves here with their basic validity but rather with their limitations and the methods of overcoming these. The great advantage of this method of testing is its independence of the patient's nervous state, and its disadvantage is its susceptibility to misinterpretation in the presence of abnormal stores of iodine—i.e., after previous treatment with either drugs or thyroid gland. This disadvantage is not overcome by any variations in the type of the test short of drug-loading procedures (see below).

Type of Test

Several types of test are available, all of which measure the rate of iodine transfer at either of two stages: (1) at the uptake by the thyroid, when it can be assessed from urine as well as from measurements at the neck; or (2) at its arrival in the plasma from the thyroid. The available comparisons of different types of uptake tests all agree that methods based on two or more measurements are more sensitive than single measurements (Keating et al. 1950, Goodwin et al. 1951, Myant 1952, Wayne 1954, Coenegracht and Fraser 1955); but single measurements are often used because of their simplicity and still retain most of the usefulness of the test.

The plasma type of test (Clark et al. 1949, Thode et al. 1954, Scott and Reilly 1954, Wayne 1954) is less versatile, requiring a larger dose of radio-iodine; its one convenience is that it requires only a single sample measurement. In the diagnosis of hyperthyroidism it may give more and not less false positives than does a thyroid-clearance measurement (Paley et al. 1955), though earlier hopes suggested otherwise (Goodwin et al. 1951), and similarly it is less useful for diagnosing myxœdema (Blom and Terpstra 1953). We have not used this test much. For general clinical purposes most variants of

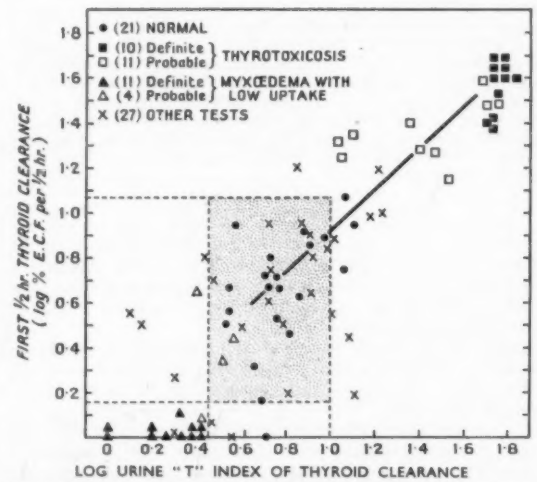


Fig. 3—Correlation between early thyroid clearance (by neck measurements) and urinary-excretion-test index thereof ("T" index). The stippled area represents the normal range.

Results are shown for group-A patients tested without preceding drugs.

Other tests = all other tests for which clinical diagnosis was uncertain; and these include examples of normal and abnormal thyroid function.

Note approximately straight-line correlation between log values of these indices. Urinary T index, being extrarenal disposal rate, never falls below a minimal value (due to non-thyroid extrarenal disposal). (From Coenegracht and Fraser 1955.)

$$\text{Urine test: } T \text{ index} = \frac{(0{\cdot}8\%) \times 100}{(8\text{–}24 \text{ hr. } \%) \times (4\text{–}8 \text{ hr. } \%)}.$$

the method of doing the test are equally valid and differ only in practical convenience.

Fig. 3 shows the good correlation between the index of thyroid uptake derived from three urine collections and direct measurement of thyroid clearance over the thyroid gland. The urine collection for the former test may be a nuisance to the patient, but errors in collection are usually revealed by the three-sample procedure. The neck clearance test takes considerably more technician-time but is needed when urine collection is difficult or suspect. The neck-thigh ratio is a less sensitive but useful simpler index of thyroid clearance but requires specialised apparatus (Pochin 1950).

Limitations of Test

One minor limitation of the test is the liability of certain types of measurement to be abnormal in the presence of renal impairment. These limitations are illustrated in two uræmic patients (table I):

Case 1, with normal thyroid function, showed normal thyroid clearance by direct measurements as well as by indexing from urine samples, though the single measurements of urine or over the thyroid are quite abnormal.

Case 2, suspected of myxœdema, showed subnormal thyroid clearance on analysis of the urine measurements; and the diagnosis of myxœdema was confirmed post mortem.

Fig. 4 illustrates a more important limitation of the test—its liability to be altered by previous treatment

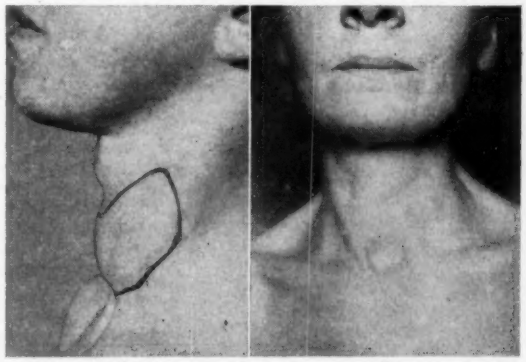
TABLE I—RADIO-IODINE TESTS IN 2 URÆMIC PATIENTS

Thyroid function	Case 1 (normal thyroid)	Case 2 (no thyroid)
Radio-iodine measurements—		
at neck:		
Early thyroid clearance of radio-iodine	3·8 % per ½ hr. (normal)	
Total at 48 hr.	80 % (similar at 4 and 8 days)	
in plasma:		
Level of protein-bound ^{131}I at 48 hr. (% dose per litre)	0·62 ± 0·2 %	
in urine:		
0–8 hr.	10·3 %	2·5 %
8–24 hr.	9·1 %	4·0 %
24–48 hr.	1·2 %	6·8 %
Total 0–48 hr.	20·6 %	13·3 %
clearances derived:		
Thyroid (K_t)	8 % (normal)	1·3 % E.C.F. per hr.
Renal (K_u)	1·8 %	0·4 % E.C.F. per hr.
Blood-urea (mg. per 100 ml.)	109	118
Necropsy finding	..	Fibrosed remnant of thyroid gland

with drugs. For instance, previous doses of iodine may easily swamp the body and so leave false indications of defective thyroid function; but these "falsely" low uptakes can be revealed by chemical estimations of the urinary iodine (Fraser et al. 1953); and these should be made whenever the uptake is defective.

The converse of this state, iodine deficiency, is one of the consequences of some months' treatment with an anti-thyroid drug and may also arise in spontaneous non-toxic goitres and in other ways. During the administration of anti-thyroid drugs the thyroid cannot fix its usual quota of iodine, and so the body steadily becomes depleted until a significant iodine deficiency develops within about two months, even though the thyroid was initially normal.

Case 3 (fig. 4A) had been receiving cobaltous chloride until ten days before the tests, when the drug was withheld because of the development of a goitre. At this time the radio-iodine test (by several techniques, including the plasma test) showed an increased thyroid uptake (like that found in hyperthyroidism), but the B.M.R. was subnormal, and scarcely any



A B

Fig. 4—A, case 3: goitrous myxœdema due to cobalt, given until ten days previously. B, case 4: goitrous myxœdema following nine months' treatment with *p*-aminosalicylic acid. In both cases there was high radio-iodine uptake with low B.M.R. and low plasma protein-bound ^{131}I.

plasma hormone was measurable chemically. Unless extra thyroid or iodine is administered to such cases, the radio-iodine tests will remain abnormal for many months.

Case 4 (fig. 4B) had been treated for nine months with *p*-aminosalicylate, and the results of the test were restored to normal after two standard loading doses of iodide. This sequence illustrates the procedure in one type of "supplemented radio-iodine test" (see below) which is used to check unexpected high radio-iodine uptakes before any inferences about thyroid function are drawn from them.

CHEMICAL ESTIMATION OF PROTEIN-BOUND IODINE

This test measures the concentration of thyroid hormone circulating in the plasma but is technically difficult. Although it is adequately sensitive and even reasonably simple it demands excessive care to keep chemicals and glassware clean for measurements at concentrations 1/1000th of those in tests usually done on blood and on plasma. Reports showing poor clinical correlations with this test probably arise mainly from this great difficulty of avoiding contamination (De Mowbray and Tickner 1952). Fig. 5 shows the accuracy of our procedure and the normal range; all estimates are duplicates, have been checked for plasma-iodide content, and are based on radio-iodine checks of the percentage distilled. The method used was a modification of that of Barker (1948). Each sample's value should be accurate to within 1 μg. per 100 ml., and changes bigger than 2 μg. per 100 ml. should be significant (fig. 5). Thus all values below 2 may be regarded as equivalent to 0 μg. per 100 ml. For the amounts concerned this is a good standard of accuracy, but for the normal range of 3·5–7·0 μg. per 100 ml. it is not very satisfactory. Mild

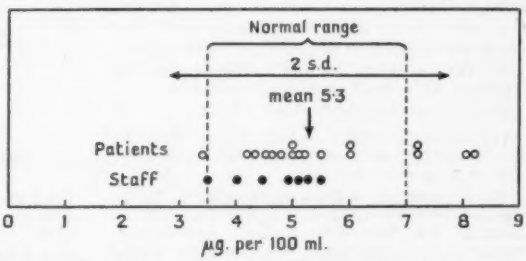


Fig. 5—Chemical measurement of plasma protein-bound ^{131}I: the normal range.

Levels are accurate to within ± 1·1 μg., and so differences beyond 1·9 μg. per 100 ml. are real; (standard error of estimation = 0·325 μg. per 100 ml.).

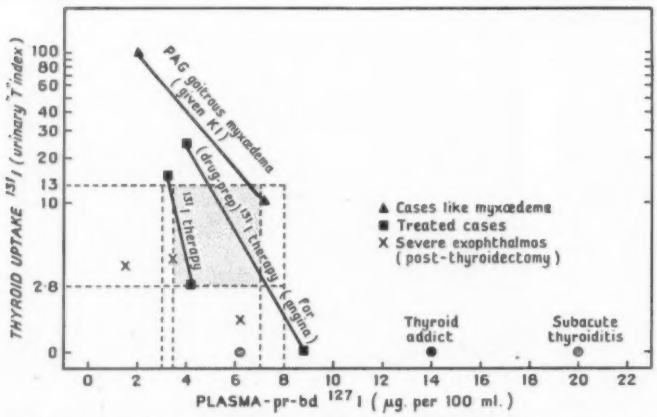


Fig. 6—Correlation between radio-iodine tests of thyroid uptake and concentration of thyroid hormone in plasma (protein-bound ^{127}I); in treated or infected thyroid disease. Hatched area represents normal range.

thyrotoxicosis may be barely outside the normal range, although the patient's radio-iodine clearance may be ten times the normal. However, used as a supplement to the radio-iodine test, the estimation can be very helpful in doubtful cases, particularly in mild myxœdema and in iodine deficiency, as shown in figs. 1, 4, 6, 9, and 10.

SUPPLEMENTED RADIO-IODINE TESTS

If we could supplement the sensitive radio-iodine test by some additions to check on either iodine loading or iodine deficiency, most of its limitations could be overcome. This is needed when the first radio-iodine test gives a result which is unexpected from the clinical picture. Such supplementing can be done in various ways.

Chemical Estimation of Iodine

Various elaborate procedures have been devised for measuring the body's iodide pool and so transforming the thyroid uptake of the radio-iodine from a percentage into an absolute figure in μg. of ^{127}I per unit time (Riggs 1952). These are unlikely to become practical clinical procedures.

A simple chemical measurement can reveal excess iodine in urine and so will probably reveal most of the abnormal results due to iodine flooding (Fraser et al. 1953), but it is unreliable for determining subnormal amounts.

In the case of other unexpected results of the radio-iodine tests a supplementary chemical estimation of the level of protein-bound iodine in the plasma may help interpretation. For example, fig. 6 shows the radio-iodine test correlated against the chemical estimation of protein-bound iodine with the range of normal values outlined. Against this background are shown the values in certain illustrative cases:

(1) A thyroid addict with no thyroid uptake but a high value of protein-bound iodine due to exogenous hormone.

(2) 2 cases of subacute thyroiditis, both without thyroid uptake, but the 1st with a normal, the 2nd with a high, circulating hormone level, the latter being the one with the more severe inflammation.

(3) 1 patient with angina of effort, with first a high radio-iodine uptake and a low-normal hormonal level due to iodine deficiency following a period of anti-thyroid drugs before the radio-iodine treatment, and later the opposite combination at nineteen days after the radio-iodine therapy, which had caused radiation damage and release of hormone.

(4) A thyrotoxic patient after similar though less intense radio-iodine therapy, showing low normal hormonal (^{127}I) levels both at one month and at eight months after treatment but minimal radio-iodine uptake at one month, and a high normal uptake at eight months, after the treatment; by which latter time the thyroid had recovered from the radiation effects.

(5) A patient with goitrous myxœdema due to *p*-aminosalicylic acid with both tests restored to near normal after the administration of iodide to correct the iodine deficiency.

RADIO-IODINE TESTS AFTER DRUG LOADING

This type of procedure is simpler for clinical practice; carefully standardised drug loading is used to circumvent the need for the more difficult chemical estimations of iodine. Two such tests have been evolved for two clinical problems: (1) the differentiation between iodine deficiency and thyrotoxicosis; and (2) the assessment of potential thyroid function after the start of treatment with thyroid.

The radio-iodine test after iodide load was designed to differentiate thyrotoxicosis from iodide deficiency, such as that which follows treatment with an anti-thyroid drug or accompanies certain non-toxic goitres. At one month after the two weeks' dosage of iodide most normal patients—e.g., the anxiety states and non-toxic goitres shown in fig. 7—will have a normal radio-iodine uptake. Most of the patients were selected for this test because they showed a high radio-iodine uptake together with, at most, dubious signs of thyrotoxicosis. At a month after the iodide dosing, at "the post-load test" the anxiety states and the non-toxic goitres showed normal uptakes, whereas the mild thyrotoxics still showed high uptakes.

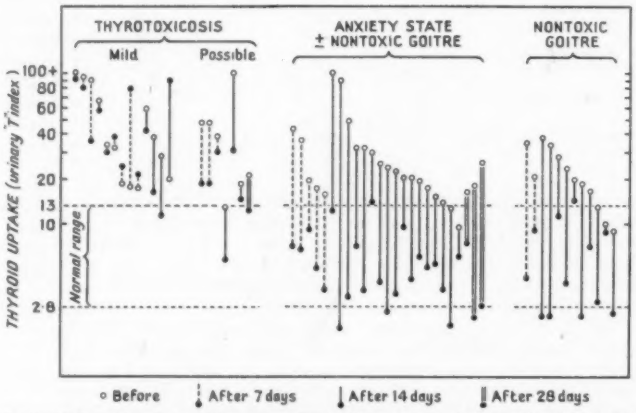


Fig. 7—Radio-iodine tests before and after iodide-loading: in hyperthyroidism and suspected hyperthyroidism.

All the untreated patients of group D have been shown. Each line connects the two tests of one patient—the hollow dot being the "pre-iodide" test, and the solid dot the "post-iodide" test. All "post-iodide" tests were made at the standard interval of one month after the iodide; the type of line joining the dots indicates the duration of the iodide load—which is for two weeks in the recommended procedure.

Note in the anxiety-state and non-toxic-goitre group the restoration to normal of the high radio-iodine uptakes (probably due to iodide deficiency) at the second test, but not in the thyrotoxic group.

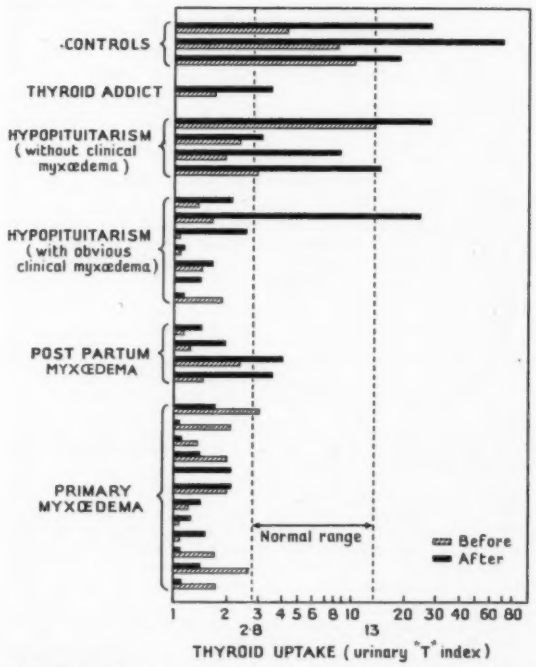


Fig. 8—Radio-iodine tests before and after five days of T.S.H. injections.

Note after T.S.H. the supranormal uptake with the control patients; the normal or supranormal uptakes with hypopituitarism without clinical myxœdema; the persisting subnormal uptake of primary myxœdema. Among the hypopituitary patients with obvious myxœdema the uptake after T.S.H. is sometimes still subnormal, suggesting combined thyroid atrophy.

Fig. 7 also shows that our standard procedure may be modified somewhat as regards the iodide load without altering the validity of the test—i.e., both a one-week load and a four-week load gave approximately equivalent results. Thus the dosage of iodide is not very critical, provided the lapse of time before the second test is standard.

A similar type of test has been devised which uses either thyroxine or thyroid (Werner et al. 1952, Greer and Smith 1954). One or two weeks' treatment with thyroid gr. 6–9 daily will suppress into the subnormal range the high radio-iodine uptakes due to iodine deficiency but not those due to thyrotoxicosis. We are at present comparing the relative value of these two types of load test for differentiating between the high uptake of thyrotoxicosis and that of iodine deficiency.

Radio-iodine tests after the administration of thyroid-stimulating hormone for myxœdema (fig. 8).—When the administration of thyroid gland has already been begun, it is still possible to find out by this test whether the thyroid tissue is potentially functional or not (Querido and Stanbury 1950, Ingbar et al. 1954, Schneeberg et al. 1954, Schultz et al. 1954). This test can also show whether the failure of the thyroid gland is secondary and due to pituitary failure.

Clinical Application of these Tests

Diagnosis of Myxœdema

Case 5 (fig. 9), while in hospital with pneumonia, was found to have a low level of protein-bound ^{127}I in the plasma. Though the result of the subsequent radio-iodine test was normal, careful clinical re-examination suggested myxœdema, which was confirmed by the therapeutic response.

It has been my experience that Simmonds's disease without associated gross myxœdema usually gives this combination of results—i.e., a normal radio-iodine uptake and a subnormal level of protein-bound iodine in the plasma (see fig. 10).

Fig. 9—Myxœdema with normal radio-iodine uptake but subnormal protein-bound ^{127}I.

Case 6.—Table II shows some similar data obtained in this case, who had mild myxœdema but was initially thought to have a non-toxic goitre. The measurements of radio-iodine at the neck indicate clearly that the radio-iodine was being rapidly discharged from the thyroid gland after an initially normal uptake. The longer-based forty-eight-hour uptake measured at the neck and the urine test show defective uptake. At operation at forty-nine hours only 21% of the dose was found in the thyroid, and histological examination showed that, except for a few isolated hyperplastic follicles, all the thyroid tissue had been converted into Hashimoto's lymphadenoid tissue.

The initial normal percentage uptake in such a case must clearly have been from an iodine-deficient pool because so few thyroid follicles had been at work.

Case 7, after a well-established clinical diagnosis of myxœdema, was found to have a goitre with a high radio-iodine uptake; but chemical estimation showed that the level of protein-bound ^{127}I in the plasma was low.

This represents one of the rare defects in which the thyroid synthesis of hormone is only to an incomplete stage which apparently does not circulate normally (McGirr and Hutchison 1955, Stanbury et al. 1955).

Diagnosis of Thyrotoxicosis

Case 8, who presented with a vascular but apparently non-toxic goitre, was found to have a high radio-iodine uptake suggesting either early toxic transformation or iodine deficiency. Chemical estimation of protein-bound ^{127}I in the plasma confirmed this suspicion of iodine deficiency, though no source of a previous anti-thyroid agent could be discovered.

TABLE II—RESULTS OF RADIO-IODINE TEST IN CASE 6 (HASHIMOTO'S LYMPHADENOID GOITRE)

Sites counted	Time	Result	Notes
Neck counts	4 hr.	25% Admin. dose (high)	Anti-thyroid drugs given from 24 to 48 hr.
	24 ,,	45% ,, ,, (normal)	
	48 ,, (pre-thyroidectomy)	22% ,, ,, (low)	
	50 hr. (post-thyroidectomy)	2% ,, ,,	
^{131}I found in removed thyroid	50 hr.	21% ,, ,,	
Urine ..	0–8 hr.	30% ,, ,,	
	0–24 ,,	31% ,, ,, (low)	
	24–48 ,,	17% ,, ,,	
	0–48 ,,	78%	
"T" index of thyroid clearance		1·3 (normal = 2·8 – 13·0)	

The post-iodide-load radio-iodine test (fig. 7) is useful with patients known to have been treated with anti-thyroid drugs. When this test was applied to thyrotoxic patients after a course of anti-thyroid drug, only those patients who later relapsed clinically showed a persistently abnormal result.

Case 9 complained mostly of severe exophthalmos but also showed nervousness and other general features raising the question of thyrotoxicosis. The suspicion of additional clinical thyrotoxicosis was confirmed not only by the radio-iodine uptake, but also by both the B.M.R. and protein-bound ^{127}I level in the plasma.

Case 10, by contrast, presented an almost similar clinical picture and also showed a high radio-iodine uptake but a normal B.M.R. and a normal level of protein-bound ^{127}I in the plasma, suggesting minimal and probably clinically insignificant thyrotoxicosis in association with the exophthalmos. Treatment of the thyrotoxicosis, under thyroxine (0·3–0·6 mg. daily) "cover" for the eyes (Fraser et al. 1953), caused little clinical change, suggesting that the nervousness was not of thyrotoxic origin.

It is interesting at this point to examine the relation between the radio-iodine uptake and the plasma level of protein-bound ^{127}I in thyrotoxicosis with and without eye signs, as shown in fig. 10. It will be noted that, where the results of these two tests deviate proportionally from the normal range, there are usually no or minimal eye signs, but most of the patients with severe eye signs tend to have more increase in the radio-iodine uptake than in the level of protein-bound iodine in the plasma. This may reflect the disproportion between the stimulation of the thyroid gland and the response to it in these cases. Thus, with severe exophthalmos the radio-iodine uptake is insufficient evidence of thyrotoxicosis to warrant any form of anti-thyroid treatment. Possibly only if the B.M.R. or the level of protein-bound ^{127}I in the plasma is also raised should patients with severe exophthalmos be given anti-thyroid treatment.

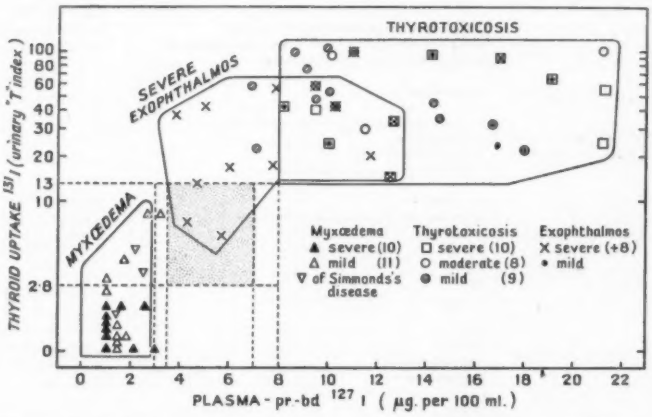


Fig. 10—Correlation between radio-iodine test of thyroid uptake and concentration of thyroid hormone in the plasma (protein-bound ^{127}I); in untreated proven thyroid disease. Hatched area represents normal range.

Note several patients with mild myxœdema, including some with hypopituitarism (Simmonds's disease) with only the protein-bound ^{127}I low; and many exophthalmos patients with only the ^{131}I uptake raised, and the latter's tendency to be disproportionately raised with severe exophthalmos.

Conclusions and Summary

We may conclude that all three types of test, properly made and interpreted, assess reliably the thyroid function of most patients.

The B.M.R. gives the best index of severity.

The radio-iodine test, in the absence of previous drugs, gives the best test for suspected thyrotoxicosis.

Chemical estimation of the level of protein-bound ^{127}I in the plasma is most useful for suspected mild myxœdema, in which the results of the other tests may be normal.

Certain modifications of these three basic tests are described which can overcome most of the limitations indicated in this comparison, particularly those due to the nervousness of the patient or to the recent administration of drugs and of thyroid gland.

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"... There are few left among us who would perpetuate the organization of independent hospitals for 'chronic' patients in the manner that still survives in too many instances to shock our sensibilities. To the relief of the social worker, who has thus far broken her heart over this problem, the general hospital is beginning to assert its rights over 'chronic' as well as 'acute,' so long as the intensive need for a hospital bed can be proved. It is, in fact, reaching out and taking under its protective wing, the bed in the patient's home in those instances where a bed in the hospital is not, or is no longer, required."—Dr. E. M. BLUESTONE (New York) in *Hospital Management*.

MITRAL VALVOTOMY
A PROGRESS REPORT

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(*concluded from p. 531*)

Intracardiac Thrombosis and Systemic Embolism

Of the 250 patients in the surgical series 48 had clot in either the left auricle or the left atrium at operation (table IV)—i.e., 19% of the whole series, and 43% of the 45 with auricular fibrillation. Hence, as has been widely recognised for many years, whatever other factors may operate, fibrillation clearly predisposes to thrombosis. Almost all these patients had tight mitral stenosis; a few had moderately severe stenosis (i.e., the valve just admitted the terminal phalanx of the surgeon's finger, although functional stenosis may have been greater); and none had significant mitral incompetence. The presence of a regurgitant jet seems to militate against thrombosis, presumably because there is less stasis than in tight stenosis. Increasing age, cardiac enlargement, and congestive cardiac failure also predispose to thrombosis, but from our observations we cannot assess other possible factors, such as roughening of the endocardial lining from the effects of rheumatic carditis, and an increase in the clotting tendency of the blood.

Of all the patients who had had systemic embolism before operation 66% had clot in either the auricle or the atrium at operation but clot was present in only 12% of those without a past history of embolism. Of those in whom clot was found 20% had systemic embolism as a direct result of the operation, despite precautions taken to prevent it. Often, when old organised clot is discovered, relatively fresh friable clot is present on its inner surface. Thus a past history of systemic embolism undoubtedly indicates an increased hazard from the operation, but it is probable (but impossible to prove in the individual case) that the risk of further systemic embolism incurred by not operating is a greater hazard.

Our experience suggests that successful valvotomy decreases the probability of further thrombosis. So far only 1 of the patients in whom clot was found at operation has had further embolism in the years following operation. In many instances it is possible for the surgeon to empty the atrium or the auricle of clot at operation before proceeding to valvotomy, but this is not possible in all cases; hence it would not be surprising if embolism were to recur occasionally. We never advised operation when embolism was the sole indication; we advised operation only when undue breathlessness was also present.

Sites of Systemic Embolism

Of the 8 patients who were known to have sustained systemic embolism as a result of operation the brain was the site in 7. Of these, 5 died from massive cerebral embolism; 1 sustained a minor motor disorder, and 1 had a quadrantic field defect. 1 patient recovered from mesenteric embolism, and 1 with hemiplegia also had embolism into the popliteal artery.

In the first 50 cases the importance of allowing gushes of blood to escape from the auricular incision before inserting the finger into the atrium was not appreciated. Subsequently, when loose clot was observed it was usually evacuated without untoward incident, but in 9 cases (20%) systemic embolism resulted. Sometimes clot which had not been detected was disturbed by the clamp placed between the auricle and the atrium. Various methods have been suggested and tried to diminish the danger of systemic embolism—e.g., manual compression of the carotid arteries in the neck, and temporary occlusion of accessible vessels by clamps or tapes. Although they are logical, there is no convincing evidence of their efficacy—i.e., of the successful redirection of clot to less vulnerable areas. Since occlusion can be maintained safely for only a minute or so at a time, one difficulty is to decide which are the best times.

Conclusion

Systemic embolism is a strong indication for considering valvotomy but also signifies a materially increased operative risk compared with cases without a history of embolism.

Calcification of Mitral Valve

Calcification was found in 27% of the patients operated on. The real incidence must be greater than this, because only those cases are included in which its presence was certain. There are obvious limitations to palpation in the living heart, and from fluoroscopy and necropsy it is clear that calcification is sometimes undetected at operation. In the great majority of cases calcification had been noted previously on radioscopy, which is the best method of examination and superior to tomography; in relatively few cases can it be seen on the X-ray films. Calcification may be present along the cusp margins, along the commissures, in the body of the cusps, or in the valve ring. Sometimes the whole valve is craggy and rock-like. Friable superficial spicules may be felt by the examining finger. Calcification may seriously interfere with the function of the valve and may be responsible for incompetence accompanying the stenosis.

The disadvantages of calcium from the operator's point of view are as follows:

(1) Widening of the orifice by effective splitting of the commissures may be impossible, and strenuous attempts to do so increase the operative risk.

(2) Good function of the valve may not be restored, even though the adherent commissures are divided.

(3) Embolism of calcified material into the systemic circulation may result and is sometimes fatal.

Calcification is also important because it modifies the physical signs of disease of the mitral valve. The first heart sound and the opening snap tend to be either inconspicuous or absent. A mitral systolic murmur tends to be loud in the presence of calcium, but in these circumstances this is of less importance in signifying an important degree of incompetence than when calcification is absent. The murmur is often high-pitched.

We have divided the degree of calcification, judged radioscopically, into three grades: slight, moderate, and gross. Table v shows that calcification is relatively uncommon but by no means unknown in the younger age-groups. It occurred most commonly in the fourth, fifth, and sixth decades, the relative incidence being greater in males than in females. Calcification occurred about equally in those with sinus rhythm and in those with auricular fibrillation. Calcification was not related to the presence of clot.

Calcification is often associated with important or predominant mitral incompetence but not necessarily so; naturally patients with such calcification were not recommended for valvotomy. Auscultation is an important guide to the relative degree of stenosis and incompetence, but, as indicated above, calcification may modify physical signs. Many patients were turned down for valvotomy on other evidence of left ventricular hypertrophy or enlargement. Of the 20 patients with the greatest amount of calcification who were operated

on none had predominant mitral incompetence and 4 had tight stenosis. 6 had moderately tight stenosis—i.e., the valve just admitted the terminal phalanx of the index finger and a regurgitant jet was felt. Of 21 patients (table v) with a moderate degree of calcification 18 had severe stenosis and 3 moderately severe stenosis. Systemic embolism occurred at operation in 8, but in 3 of these friable clot was also present and considered by the surgeon to be the source of the embolus.

Results

Of 41 patients (table v) with either severe or moderately severe calcification of the mitral valve 2 with very large hearts died at operation from cardiac arrest; 2 others with large hearts died a few days after operation from cardiac failure; 2 died from calcific cerebral embolism; and 3 sustained small calcific emboli but fortunately without serious after effects, and in each case satisfactory division of the commissures was obtained.

Of the 32 survivors who have been followed up for more than a year the functional result has been classified as good in 23, fair in 5, and poor in 4.

Conclusion

It is therefore evident that heavy calcification increases the operative risk from systemic embolism and to some extent militates against a good functional result, but nevertheless a good result is obtained in most patients, and even severe calcification does not contra-indicate operation.

Associated Cardiac Defects

Mitral Incompetence

One of the principal tasks in the assessment of patients for mitral valvotomy is to try and ensure that an important degree of mitral incompetence is not associated with the stenosis. Significant incompetence may coexist with mild or moderate stenosis but is incompatible with severe stenosis. Associated incompetence increases the effect of the stenosis in reducing left ventricular output into the aorta. Considerable incompetence precludes a good operative result not only because it indicates rigidity and deformity of the valve but also because, in our experience, it has never been conclusively reduced by valvotomy and the patient may be made worse. There is no satisfactory operation for mitral incompetence and probably there never will be, because in such cases there is so often severe rheumatic myocardial damage.

In medical practice absolute reliance can rarely be placed on a single sign, and in this context there are no absolute rules, because it is possible to cite from personal experience an occasional exception to every generalisation. In this age of elaborate investigations and highly specialised techniques it is interesting to have reached the conclusion that, as regards the problem of mitral incompetence, the wheel has turned full circle; that eyes, hands, and ears have come into their own again; and that clinical examination of the patient usually gives more valuable information than do special tests in a practical problem of major importance. Electrocardiography is useful, but radiography may be misleading. Very occasionally, when the disability is severe and progressive and certain diagnosis cannot be achieved with confidence, exploratory cardiotomy may be justified, but this necessity should be rare. By paying meticulous attention to each sign very considerable accuracy can be achieved.

In summary, a weak or absent first heart sound or snap that cannot be attributed to a calcified or rigid mitral valve with tight stenosis, a loud harsh systolic murmur, maximal at the apex and heard towards the axilla, that cannot be attributed to aortic stenosis or tricuspid incompetence, and any evidence of left ventricular hypertrophy that cannot be attributed to aortic valvular disease almost invariably signify an important degree of mitral incompetence. There may also be an apical systolic thrill, no presystolic murmur, and a mid-diastolic murmur that is short. A third heart sound may occur with severe incompetence, but it may also occur in mild stenosis without incompetence in a young person. We have not found analysis of the radial pulse to be helpful.

Aortic Stenosis

9 patients (6 in this series) with evidence of severe aortic stenosis and severe mitral stenosis have now been subjected to both aortic valvotomy and mitral valvotomy. The first patient was operated on for mitral stenosis in the first instance and for aortic stenosis six months later, but the remainder were treated for both defects at the same thoracotomy (Logan and Turner 1953). In such instances it is, of course, impossible to assess the relative degrees of improvement due to each operation, but in our experience the over-all improvement may be very considerable, and we have no reason to believe that the operative risk is increased by the double operation.

Aortic Incompetence

Mild or moderate aortic incompetence does not contra-indicate valvotomy for associated severe mitral stenosis, and we have had excellent results in this group. An early diastolic murmur from pulmonary incompetence only occurs with considerable pulmonary hypertension. Such a murmur may be impossible to differentiate from one due to aortic incompetence; the only certain criterion is its disappearance after successful valvotomy. A constant diastolic pressure of 60 mm. Hg or more excludes an important degree of aortic incompetence. We have not yet attempted to deal with aortic incompetence.

Tricuspid Disease

Significant organic defects of the tricuspid valve are usually associated with severe rheumatic heart-disease, and we have not yet tried to operate on them.

Functional tricuspid incompetence is common in patients with mitral stenosis and cardiac failure.

Atrial Septal Defect

An atrial septal defect associated with mitral stenosis (Lutembacher's syndrome) may alleviate symptoms due to the valvular defect by reducing pulmonary hypertension, and in future both defects should probably be dealt with at the same thoracotomy with the aid of hypothermia. Meanwhile the diagnosis of Lutembacher's syndrome should not contra-indicate valvotomy for tight mitral stenosis. One of our patients with a severe disability has maintained striking symptomatic improvement for more than two years despite a persistent septal defect 3 cm. in diameter.

Cardiac Cirrhosis of Liver

Engorgement of the liver is the inevitable consequence of congestive cardiac failure; when failure is recurrent or persistent, and especially when it is accompanied by tricuspid disease, cirrhosis gradually develops. With the enormous reserve capacity of the liver impairment of hepatic function may not be evident for some time, although it may contribute to malnutrition and loss of weight. Histological studies show that most of the liver-function tests in common use (plasma-proteins, serum-bilirubin, alkaline phosphatase, flocculation tests, and urobilinogenuria) remain normal until a late stage. The most delicate of the common tests is that of bromsulphthalein excretion. Nevertheless, from the practical point of view, considerable hepatic enlargement which is due to persistent engorgement and does not respond to satisfactory treatment for congestive failure, judged by the disappearance of peripheral œdema and increased

venous pressure, is a sign that the liver has been seriously and permanently damaged.

Valvotomy in Pregnancy

In patients with mitral valvular disease symptoms often appear for the first time during pregnancy and often surprisingly early—e.g., within a few weeks of conception. Severe symptoms—e.g., acute pulmonary œdema and profuse hæmoptysis—not infrequently develop in a woman with relatively mild mitral stenosis in whom undue breathlessness on exertion was not present before pregnancy. We have previously reported 3 cases subjected to valvotomy during pregnancy (Logan and Turner 1952a): 2 others have since been treated in the same way. Our present view is that the operation should be done, preferably about the fourth month, in those in whom it is clear, from a history of progressive dyspnœa before pregnancy, that valvotomy would have been advised in any case, and in those in whom there is unequivocal evidence of tight stenosis—i.e., those with physical signs of pure mitral stenosis and electrocardiographic signs of right ventricular hypertrophy. Operation not only safeguards the heart during the remainder of the pregnancy and during the strain of labour, but also saves the mother from subsequent separation from her baby while valvotomy is done. In other cases the patients can be successfully shepherded through pregnancy and parturition with the aid of the customary measures for treating and preventing cardiac failure and with extra rest. Many patients not only date the onset of their symptoms from pregnancy but also consider that subsequently they never regained their former exercise tolerance. We have no reason to believe that valvotomy during pregnancy carries an added risk to the mother, but probably there is an increased likelihood of miscarriage.

Patients for whom Operation was not Advised

The proportion of patients needing operation cannot be assessed from this series, because many were referred with the possibility of operation in view and others were referred from special departments, such as antenatal clinics and medical boards, because of a murmur. A similar number of patients (250) were seen in about the same period and not advised to undergo surgical treatment:

115 were considered unsuitable because the condition was too mild or non-progressive, judged by symptoms and by negative evidence of pulmonary hypertension on clinical examination, radiography, and electrocardiography, and (sometimes) cardiac catheterisation.

135 patients were considered unsuitable because the mitral stenosis was too severe—e.g., gross cardiac enlargement with intractable congestive failure—or because of some important complicating factor—e.g., mitral incompetence, aortic valvular disease, systemic hypertension, and pulmonary disease. A past history of cerebral embolism which had caused a disabling hemiplegia precluding any possible improvement in effort capacity was the principal contra-indication in some cases. In many instances more than one contra-indication existed.

So far in very few cases classified as too mild for valvotomy was there any need to reconsider the decision because of the development of symptoms suggesting increasing stenosis—i.e., where previously there had been no evidence of progression there was rarely any progression subsequently.

Indications for Operation

Except as regards errors of judgment related to cardiac enlargement or to associated mitral incompetence, we consider that the selection of cases in this series was justified. 97% had tight (finger-tip) or fairly tight (terminal phalanx) stenosis, and in this group it is difficult to believe that the natural history of mitral stenosis without operation would have been other than a continuation of the progressive downhill course which was evident before operation. Since it is impossible to predict what the surgeon will be able to achieve, there must inevitably be some disappointments, but in this series 87% of the survivors are satisfied that the operation was well worth while, and very few indeed regret the attempt. Fair or poor results were usually due either to poor selection or to an excessively rigid valve, with consequent difficulty in splitting the commissures, or to the production of traumatic mitral incompetence. In only 1 case was the mitral stenosis too mild for valvotomy to be profitable.

Until better technical results can be achieved through ability to operate on the dry heart under direct vision, improvement in the proportion of good results can only be achieved by eliminating those patients in whom the chances of a good result are relatively slender. However, such a rigid selection would inevitably mean that a new lease of life would be denied to many.

Operation should be considered in every case of mitral stenosis in which the symptoms are either severe or progressive. Most patients are operated on too late—i.e., when the optimal time has passed. Analysis of the last 100 consecutive patients—i.e., since the value of the operation has been thoroughly established—shows that, judged by the history, operation was usually considered about three years too late. During this time the indications for considering operating should have been apparent to the examining physician. The heart had had to work against a severe mechanical obstruction to its obvious detriment and with a consequent lessening of the chances of a good operative result. However, the problem is not always a question of the duration of symptoms, because the operative result is largely determined by the local pathological anatomy of the mitral valve, and, as we have emphasised, there is no sure way of determining this in advance. Probably some valves are never at any stage anatomically suitable for valvotomy, because of rigidity of cusps and shortening and fusion of chordæ.

We emphasise that progressive symptoms warrant consideration of operation even if they are not severe.

Operation may be urgent. For some time, when there were many patients awaiting treatment, the mortality among those on the waiting-list was greater than in those undergoing operation, and this was only reduced by a better appreciation of relative priorities. Pulmonary œdema is a danger sign, as is pulmonary infarction, which is probably usually due to local thrombosis in the pulmonary arterial tree. In our experience there has very rarely been evidence of thrombosis in a peripheral vein.

With increasing experience the problem becomes more, rather than less, difficult. Since most patients receive substantial benefit from operation, one is naturally anxious to offer the opportunity of improvement to many who are seriously disabled, even though there are relative contra-indications. These include age over 50, considerable cardiac enlargement, congestive failure, mitral incompetence, aortic valvular disease, calcification of the mitral valve, and unrelated pulmonary disease. Probably the only absolute contra-indications are age over 60, gross cardiac enlargement, intractable cardiac failure, cardiac cirrhosis of the liver, and predominant mitral incompetence.

In the assessment the physician must consider the degree to which the symptoms can be attributed to the mechanical effects of obstruction at the mitral valve, the degree to which the present incapacity limits the type of life the patient wishes to live, including sometimes the advisability of pregnancy, the probable prognosis as regards life without operation, and the operative risk. There is a considerable group of patients in whom the decision is difficult and debatable, and a calculated

risk has to be accepted where surgery is advised. Sometimes the doctor must assume the responsibility—i.e., when the factors are such that the patient cannot appreciate the issues involved (e.g., the hazards of clot and of calcification). On other occasions, with the issues before him, the patient must take the decision—e.g., in the presence of a reasonable chance of worth-while but not dramatic improvement, a moderate risk of failure to obtain such improvement, and a possibility that the condition may be made worse. This particularly applies to the older age-groups and those with big hearts, congestive failure, or mitral incompetence. Excellent symptomatic results, at least for a time, may be achieved in such cases, but the chances of improvement are relatively small and the risk of failure or disaster is relatively great. For the individual patient in this group the prognosis is very difficult.

Controversial Issues

Since experience with mitral valvotomy is everywhere limited to a few years, it would be invidious to criticise current views of other workers. Therefore it is sufficient to state where our experience appears to differ.

American Heart Association classification.—The A.H.A classification of cardiac disability is widely used and said to be a good guide to the selection of cases for operation, but it deals only with symptoms and takes no account of the many variable factors which may contribute to the disability—e.g., cardiac enlargement, rhythm, associated mitral incompetence, aortic valvular disease, bronchitis, and anxiety. For these reasons we have not found the classification helpful in assessing suitability for operation.

Age.—Some workers have stated that patients should not be operated on after the age of 45, and others that operation should not be denied because the patient is aged more than 50, since the mortality and morbidity are comparable to those in the young age-groups. Our experience suggests that age is no barrier to operation and the attainment of good results, but the over-all mortality is considerably higher in those aged more than 50 and the number of good results fewer. 69 patients aged more than 45, including 29 aged more than 50, were operated on.

Auricular fibrillation.—The presence or absence of auricular fibrillation is often said to be immaterial. In our experience fibrillation increases the operative risk and decreases the chances of a lasting good result (table II).

Embolism.—It is said that a past history of embolism into the systemic circulation is commonly associated with mitral incompetence, and that in such cases clot is no more likely to be found than in those without such a history. In our experience clot is far more common in those with tight mitral stenosis than in those with either pure or predominant incompetence, and it is far more likely to be present in those with, than in those without, a past history of embolism.

Aortic valvular disease.—Aortic stenosis and aortic incompetence are usually given as definite contra-indications to mitral valvotomy. However, even severe aortic stenosis should no longer be a contra-indication, because it can be dealt with at the same thoracotomy, and we have done this successfully in 9 patients. In the absence of peripheral signs it is not always possible to distinguish an early diastolic murmur due to aortic incompetence from one due to functional pulmonary incompetence; but if the murmur either persists or increases after successful mitral valvotomy it may reasonably be attributed to aortic incompetence. In this series aortic incompetence was present in about 30%.

Pulmonary infarction.—Peripheral thrombophlebitis has been claimed as the usual cause of pulmonary infarction in patients with mitral stenosis. In our experience a peripheral source of pulmonary embolism was rarely found; it therefore seems more probable that infarction is usually due to thrombosis in the pulmonary arterial tree in patients with severe congestion.

Pulmonary infarction with persistent pleural effusion.—It is still insufficiently recognised that pulmonary infarction may be associated with pleural effusion that persists for months. Much time is spent in unnecessary investigation for pulmonary tuberculosis or, because of the pyrexia, for bacterial endocarditis. Since the pulmonary infarction is associated with tight stenosis, and the prognosis without operation is poor, operation should not be delayed.

Digitalis.—It is usually advised that digitalis should be given as a routine before operation. We have not considered it necessary in patients in sinus rhythm and so far have had no reason for regret.

Anticoagulants.—It has been recommended that heparin should be given in the early postoperative days if clot is found at operation. This seems unnecessary because in our experience (without heparin) systemic embolism never occurred in this period.

Radiology.—It is still claimed that systolic expansion of the left atrium is a good guide to mitral incompetence, that predominant mitral incompetence inevitably leads to much enlargement of the left atrium, and that auricular fibrillation leads to atrial enlargement. We consider that systolic expansion of the left atrium, even when clearly seen in the anterior and oblique views is of no practical value in diagnosis, because, though less commonly, it may be seen in patients with either pure or predominant mitral stenosis and may be absent in patients with free regurgitation; that predominant mitral incompetence may be found with but little enlargement of the left atrium; and that auricular fibrillation does not necessarily lead to atrial enlargement unless congestive failure is also present. It has been claimed that narrowing and irregularity of the peripheral branches of the pulmonary artery are a good guide to the degree of pulmonary hypertension. In our experience there are many discrepancies. Absence of enlargement of the pulmonary artery and right atrium and clear lung fields are said to be incompatible with tight stenosis, but we have met with exceptions.

Cardiac catheterisation.—It has been said that catheterisation is of value because pulmonary hypertension is difficult to assess clinically, and that it is the best guide to the selection of patients likely to benefit from valvotomy; that a normal pulmonary arterial pressure with tight stenosis invariably signifies active carditis; and that patients with large hearts have higher pressures. In our experience pulmonary hypertension can usually be assessed clinically by symptoms (e.g., pulmonary œdema with sinus rhythm), by signs (e.g., well-marked accentuation of the pulmonary second sound and a right ventricular heave), by radiography (e.g., well-marked enlargement of the pulmonary artery, and dilated lymphatics), and by electrocardiography (e.g., the pattern of right ventricular hypertrophy). There are no absolute rules, and exceptions occur as regards individual signs, but the combination of signs is accurate for practical purposes in most cases, and catheterisation rarely influences the decision reached on clinical grounds, though it may be of value in doubtful or complex cases. Normal pressure may likewise reflect severe but inactive myocardial disease, and (probably for the same reason) people with large hearts do not always have pulmonary hypertension. Catheterisation is uncomfortable, potentially dangerous, and unnecessary in most cases. Inaccurate conclusions may be drawn from observations on a single occasion, owing to anxiety, an unusual heart-rate, difficulty in reproducing a constant degree of exercise, and technical errors. It is a poor guide to mitral incompetence. We have yet to meet an

instance where cardiac catheterisation has proved of decisive value in differentiating predominant incompetence from stenosis, and it may be misleading.

Reduction of mitral incompetence.—It has been claimed that mitral valvotomy often either reduces or eliminates an associated regurgitant jet. In our experience mitral incompetence has never been convincingly influenced in this way.

Summary

250 patients from one medical unit who were subjected to mitral valvotomy have been analysed as regards various factors which may influence the operative result.

These patients were followed for more than twelve months, 202 for more than two years, 116 for more than three years, 37 for more than four years, and 9 for more than five years.

97% had either tight (finger-tip) or fairly tight (terminal phalanx) stenosis.

The patients were aged 16–60, and 29 were aged more than 50.

44% had auricular fibrillation, 27% had calcification of the mitral valve, and in 19% intracardiac clot was found at operation.

250 other patients with mitral stenosis were seen in about the same time and not advised to have an operation, because their condition was either too mild, too severe, or complex.

The concept of the "pliant" or "diaphragmatic" valve is reviewed. In this series such a valve was uncommon and often unpredictable by auscultation.

Absence of an opening snap signifies either calcification, a rigid valve, or predominant mitral incompetence.

The electrocardiographic signs of right ventricular hypertrophy are summarised, and the value of right-side V leads is pointed out. In association with signs of uncomplicated mitral stenosis evidence of right ventricular hypertrophy invariably indicated that the stenosis was sufficiently severe to warrant operation.

Some of the radiological aspects of mitral disease which are of particular importance are discussed, and emphasis is laid on the significance of the transverse lines, which are believed to indicate distended lymphatics.

Cardiac catheterisation is rarely required in the assessment for operation, and its limitations are pointed out.

The operative risk is discussed, and causes of death are analysed.

The over-all operative mortality was 8%. In patients aged less than 50, even with auricular fibrillation and moderate enlargement, it was 5%. In all age-groups with a cardiothoracic ratio less than 60% the mortality was 3%, and in patients with sinus rhythm the over-all mortality was only 1%. There have been only 2 deaths in the last 100 cases.

Subjective evidence of improvement is difficult to assess.

Electrocardiographic evidence of regression of the pattern of right ventricular hypertrophy is the least equivocal objective sign.

The results were either good or very good in 70% of the series and fairly good in 10%—i.e., worth-while results were obtained in 80%.

Poor results are analysed in detail. Systemic embolism, inadequate valvotomy, and traumatic mitral incompetence are the surgical factors concerned. Medical factors include poor selection from excessive cardiac enlargement, associated mitral incompetence, active rheumatic carditis, and unrelated pulmonary disease.

Postoperative auricular fibrillation developed in 24% of patients previously in sinus rhythm. Normal rhythm was restored in all but 2 of the 34 cases.

Postoperative retention of fluid with increased venous pressure and peripheral œdema was common but disappeared spontaneously without treatment in most cases.

The postoperative pyrexial syndrome is reviewed, and it is concluded that, in most cases, recrudescence of rheumatic fever is not the cause, but the clinical manifestations are due to a postoperative systemic disturbance with pericarditis and pleuritis.

Re-stenosis is considered to be rare. 5 patients were subjected to a second valvotomy, but the evidence suggests that the recurrence of symptoms was due to an inadequate first attempt in the early days and not to re fusion of the divided commissures.

Except 5 patients in whom the valvotomy was repeated and 4 who developed unrelated complications, deterioration followed operation in 13 patients. In 6 the initial postoperative grading was good, in 6 it was fair, and in 1 it was poor. In most of them the course was that of progressive cardiac failure, sometimes initiated by the onset of auricular fibrillation, and amounted essentially to progression in the natural history of advanced mitral stenosis.

7 of the patients died subsequently 1–39 months after operation.

The larger the heart the less likely is a good operative result to be achieved or maintained, and the least hopeful combination is a large heart with auricular fibrillation and without electrocardiographic evidence of right ventricular hypertrophy.

In patients aged more than 50 there is a high incidence of auricular fibrillation, considerable enlargement, calcification of the valve, and intracardiac clot; consequently the operative risk is greater and the proportion of good results smaller. Nevertheless a good result was obtained in 60% of 29 patients aged more than 50, and in 7 of 8 patients without these adverse factors.

The incidence of auricular fibrillation increases with age and with heart size. It was present in 43% before operation. Disadvantages of fibrillation are a higher incidence of intracardiac clot, of operative deaths, and of limited success.

Clot in either the left auricle or the left atrium was found at operation in 43% of patients with auricular fibrillation but in only 2 patients with sinus rhythm. It was present in two-thirds of those who gave a past history of systemic embolism but in only 12% of those without such a history. Systemic embolism occurred at operation in a third of those in whom clot was found.

The mitral valve was calcified in 27% of the patients who came to operation. Its incidence increased with age and was greater in males. Disadvantages of calcification from the operator's point of view are that effective splitting of the commissures may be impossible and attempts to achieve this increase the operative risk, good function of the valve may not be achieved despite good splitting of the commissures, and calcific embolism may take place into the systemic circulation. Despite these facts good results were obtained in more than half the patients with severe calcification. Calcification also modifies physical signs. The first heart sound and opening snap tend to be inconspicuous or absent, and a mitral systolic murmur may be loud and harsh without important mitral incompetence.

Predominant mitral incompetence should rarely be a surprise at operation. In the diagnosis of mitral incompetence the customary methods of examination are still of greater value than new techniques.

Aortic stenosis does not contra-indicate mitral valvotomy for mitral stenosis, because aortic valvotomy can be carried out at the same thoracotomy. This was done in 6 patients in the present series.

Severe cardiac cirrhosis of the liver is considered to contra-indicate operation.

In pregnancy severe symptoms may develop with only moderate stenosis. 5 patients were subjected to valvotomy about the fourth month. Operation is advised only if it is clear from the history that there was pro-

gressive dyspnœa before pregnancy and that valvotomy would have been indicated in any event, and in those with unequivocal evidence of tight stenosis in the form of the appropriate physical signs together with electrocardiographic evidence of right ventricular hypertrophy. Pregnancy may permanently aggravate the symptoms.

Although the operative result is largely determined by the local pathological changes in the mitral valve, it is clear that most patients are still being referred for operation after the optimal time has passed, judged by symptoms.

Operation should be considered whenever symptoms are progressive, and done unless contra-indications are present.

Relative contra-indications to operation include age over 50, considerable cardiac enlargement, recurrent cardiac failure, mitral incompetence, calcification of the mitral valve, aortic valvular disease, and unrelated pulmonary disease.

Absolute contra-indications include age over 60, gross cardiac enlargement, intractable cardiac failure, cardiac cirrhosis of the liver, and predominant mitral incompetence.

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INFECTION OF VOLUNTEERS BY A VIRUS (A.P.C. TYPE 1) ISOLATED FROM HUMAN ADENOID TISSUE

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DURING recent years evidence has accumulated that the viruses which have been termed adenoidal-pharyngeal-conjunctival agents (Huebner et al. 1954) or A.P.C. viruses* (Rowe et al. 1955), are associated with acute respiratory disease in man. Rowe et al. (1953) described, under the name of adenoid-degeneration agent, a virus belonging to this group which they isolated from human adenoids undergoing spontaneous degeneration in tissue-culture. Hilleman and Werner (1954) reported the isolation of a new agent, which they called RI-67, from patients with acute respiratory illness and referred to presumptive evidence of an immunological relationship between RI-67 and the adenoid-degeneration agent. The studies of Huebner et al. (1954) resulted in the delineation, on the basis of cross-neutralisation tests with rabbit antisera, of 6 immunological types of A.P.C. virus, to one or other of which the previously described agents could be assigned. In the course of their studies these workers administered all 6 types of virus to volunteers. Few clinical manifestations were observed, but in most of the volunteers sharp rises in complement-fixing and neutralising antibody levels and the recovery of virus from nasopharyngeal secretions taken three to six days after administration indicated that infection had occurred.

The RI-67 strain, which was the first virus of the group to be found in association with human disease, was subsequently designated by Huebner et al. (1954) as the prototype of type-4 A.P.C. virus. Further evidence of an ætiological relationship between RI-67 infection and acute respiratory disease was obtained in serological studies by Dingle et al. (1954). Type-3 A.P.C. virus was recorded (Parrott et al. 1954) in association with an outbreak of acute febrile pharyngitis and conjunctivitis—a syndrome to which the term pharnygo-conjunctival fever was later applied (Bell et al. 1955). Ward et al. (1955) described the occurrence of pharyngo-conjunctival fever after the combined pharyngeal and conjunctival administration of type-3 or type-4 A.P.C. virus.

The studies so far reported of the association of A.P.C. virus infections with human disease have been concerned mainly with type-3 or type-4 infections. The present paper deals with experimental human infections by a strain of type-1 A.P.C. virus. The work was carried out with the help of eleven adults who volunteered specifically to take part in this investigation, with the knowledge that some of them might experience a febrile respiratory illness. The material which was administered to them was obtained by direct passage of the virus from a culture of human adenoid tissue into cultures of embryonic human kidney tissue.

Clinical Methods

The volunteers were admitted to Harvard Hospital, Salisbury, on May 10, 1955. At the time of their arrival a preliminary inspection was made for signs of respiratory infection. After a communal lunch the conduct of the proposed investigation was described to them by the medical officer. The volunteers were told that some, or possibly all, of them would be given material containing live virus but that neither the clinical observer nor the volunteers would be informed what material had been given to any individual member of the group until the clinical assessments had been completed at the end of their stay at the hospital.

The volunteers were then placed in isolation accommodation, either singly or in groups of two or three. A thorough medical examination, including radiography of the chest, was made of each volunteer in order to ensure general fitness for participation in the investigation. The matron and the clinical observer visited the volunteers, while in isolation, once daily as a routine and more frequently as the necessity arose. The volunteers made written reports each morning of any symptoms during the preceding twenty-four hours. Observations for signs of respiratory infection were made daily by the clinical observer. The mouth temperature was recorded twice daily and the resting pulse-rate each morning.

On May 12 the virologist administered to all the volunteers culture material containing a strain (ADS 17) of type-1 A.P.C. virus. The volunteers were made to lie on their backs, with the head and neck fully extended, and the material was dropped into the nose. The same dose of 1 ml. (0·5 ml. into each nostril) was given to all. The volunteers remained in isolation until May 19 and returned to their homes on May 20. Before their departure they were each provided with a postcard, on which was printed a questionnaire relating to subsequent respiratory symptoms, and were requested to complete and return this after an interval of two weeks. All the volunteers complied with this request.

* The nomenclature of this group of viruses was still under discussion when the present paper was submitted for publication. Agreement has now been reached (see *Science*, 1956, 124, 119) on the term "adenovirus group."

Garglings for virological study were collected from all the volunteers before administration of the culture material and on the second, fourth, and sixth days after administration. Blood for serological examination was taken from each volunteer, one specimen before administration of the culture material and one specimen about four weeks later. Nose and throat swabs for bacteriological investigation were taken from all the volunteers at the time of their arrival and from those who later developed signs of respiratory infection.

Laboratory Materials and Methods

Sources of Virus Strains

A.P.C. virus strains of types 1, 2, 3, 5, and 6 were received from Dr. R. J. Huebner, National Institutes of Health, Bethesda, Md, and of type 4 (strain RI-67 of Hilleman and Werner 1954) from Dr. A. P. Goffe, Central Public Health Laboratory, Colindale, London. These strains were propagated in our laboratory in cultures of HeLa cells and stored at –20°C.

Strain ADS 17, which was used in the present investigation, was one of a number of strains isolated at this unit from human adenoid tissues. The adenoids, removed at routine surgical operations on young children, were kindly supplied to us by Mr. Brian Reeves, Salisbury General Hospital.

Tissue-cultures

Adenoid tissue and embryonic human-kidney tissue were cultivated in roller-tubes by the methods employed by Rowe et al. (1953). HeLa cells were maintained and used for virus propagation by techniques described elsewhere (Pereira 1956).

Isolation of Virus from Adenoids

Fluids from cultures of adenoid tissues were transferred to cultures of HeLa cells and to cultures of embryonic human-kidney tissue. Cultures showing typical cytopathic changes were selected for further study. The HeLa-cell cultures were used only for subsequent laboratory investigations. Their total contents were homogenised in a TenBroeck grinder and centrifuged to remove cellular debris, and the supernatant fluids were stored at either –20°C or –76°C.

Preparation of Virus for Administration to Volunteers

The material which was administered to the volunteers was the fluid phase from a first passage of strain ADS 17 in cultures of embryonic human-kidney tissue. This material, which was stored at –76°C, had a titre in cultures of HeLa cells of $10^{7\cdot2}$ 50% tissue-culture doses ($T.C.D._{50}$) per ml. and was bacteriologically sterile. It was diluted to 10^{-3} in broth-saline, and 1 ml. of this dilution, containing $10^{4\cdot2}$ $T.C.D._{50}$, was administered to each volunteer.

Isolation of Virus from Volunteers

Garglings from volunteers were collected in 10% tryptic digest broth in normal saline. These were stored at –20°C and tested for the presence of virus by the inoculation of 0·1 ml. volumes into groups of three or four cultures of HeLa cells. The cultures were examined microscopically every two or three days for cytological changes. As long as no typical cytopathic effect was observed the fluid was replaced by fresh medium at weekly intervals. Observation of cultures showing no cytopathic effect was discontinued after three weeks' incubation.

Identification of Virus Strains

Strain ADS 17 and the viruses which were isolated from the volunteers were identified and typed by means of serum-neutralisation and complement-fixation tests using rabbit antisera. Details of the methods are described elsewhere (Pereira 1956).

Examination of Blood-sera from Volunteers

Specimens of blood were taken from volunteers for serum-neutralisation and complement-fixation tests. The sera were separated, inactivated at 56°C for thirty minutes, and stored at –20°C. Paired sera from any individual were always tested in parallel.

For the *serum-neutralisation tests*, mixtures of equal volumes of serial dilutions of serum and of a virus dilution containing about 10^4 $T.C.D._{50}$ per ml. were made up in HeLa-cell test medium (Pereira 1956). The tubes were incubated for an hour at 37°C and the contents added to groups of two or three cultures of HeLa cells, in quantities of 1 ml. per culture. In the virus control cultures, which were inoculated with the same dose of virus, cytopathic changes began usually on the third or fourth day of incubation. The result of each test was read three days after the appearance of cytopathic changes in the virus control cultures. Neutralisation titres were expressed as the reciprocal of the highest final dilution of serum in the mixtures which completely inhibited cytopathic effect.

The antigens used in the *complement-fixation tests* were prepared for each of the 6 types of A.P.C. virus from cultures of HeLa cells inoculated with the appropriate type strain. Cultures showing advanced cytopathic effect were ground in a TenBroeck grinder and centrifuged at low speed, and the supernatants, heated at 56°C for thirty minutes, were used as antigens. The optimal dilution of each of the six antigens was determined by chess-board titrations against the post-administration serum from volunteer L. The tests were performed in 'Perspex' hæmagglutination plates using a unit volume of 0·025 ml. delivered from a calibrated dropping syringe. Serial twofold dilutions of the sera were tested against the optimal dilution of each of the six antigens in the presence of 2 units of complement. The plates were held overnight at 4°C in 'Polythene' bags. They were then placed in an incubator at 37°C for thirty minutes, after which 0·025 ml. of a hæmolytic system, consisting of a 2% suspension of washed sheep cells sensitised by 2 units of hæmolysin, was added. The plates were reincubated at 37°C for thirty minutes and shaken by hand at ten-minute intervals. The result was read after a further period of two hours at 4°C. Titres were given as the reciprocal of the initial serum dilution showing 50% fixation. When not observed directly the titre was calculated by interpolation. The diluent used throughout the complement-fixation tests was a 0·85% solution of NaCl in glass-distilled water.

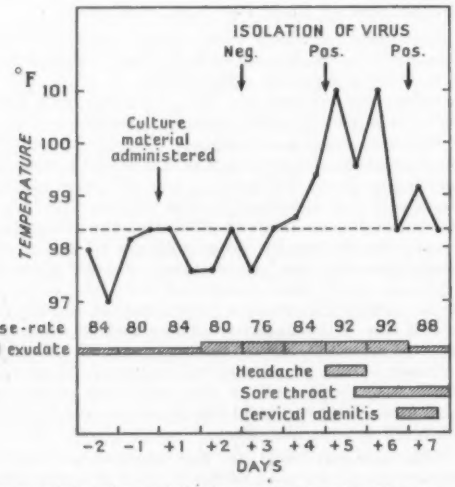
Clinical Findings

The distribution of the volunteers in their isolation quarters was as follows:

A.—Woman, aged 27, in single isolation.
B and C.—Women, aged 23 and 25.
D, E, and F.—Women, aged 29, 35, and 35.
G and H.—Married couple: husband aged 31, wife aged 24.
J, K, and L.—Men, aged 25, 32, and 39.

Throughout the period of observation before the administration of the culture material all the volunteers were in good health and none of them had symptoms or signs suggestive of acute respiratory infection. All the men (G, J, K, and L) had moderate amounts of clear nasal exudate, which were considered to be within the limits of normal, while the women had little or no appreciable nasal exudate.

The culture material was administered to the volunteers at about noon on the second day after their arrival. The time of administration is represented in this section by "d" and the successive periods of twenty-four hours which followed are represented by d+1, d+2, &c., days.



Summary of clinical record of volunteer J. Days start at noon.

Volunteers A, B, C, D, E, and *F* remained in good health throughout the period of isolation and developed no symptoms or signs suggestive of respiratory infection.

Volunteer G complained of nasal stuffiness and dryness of the mouth on d + 1 and of transient slight sore throat on d +.2 and d + 3. No further symptoms or signs developed.

Volunteeer H had no symptoms, but on d + 4 a small amount of mucoid postnasal discharge was observed.

Volunteer J showed, on d + 2, a slight increase of nasal exudate which persisted until d + 6. Towards the end of d + 4 the mouth temperature was 99·4°F and by the same evening (d + 5) had risen to 101°F. During the afternoon headache developed, and after a feverish night the patient awoke with a sore throat. The pharynx and fauces were not noticeably inflamed and no pharyngeal or tonsillar exudate was observed. On d + 6 one of the cervical lymph-nodes, near the angle of the left side of the jaw, was found to be tender and slightly enlarged. By the end of d + 7 the temperature had returned to normal and the cervical adenitis had subsided. On the morning of departure (d + 8) the volunteer's general condition was good and his only symptom was slight sore throat, which persisted for three days after he had left the hospital. The accompanying figure summarises the clinical record of this volunteer during the period of isolation and indicates the results of the examination of garglings for the presence of A.P.C. virus.

Volunteer K complained of lassitude on d + 3, slight headache on d + 5, and slight nausea on d + 6. He remained apyrexial, and there were no symptoms or signs suggestive of respiratory infection.

Volunteer L remained in excellent health until d + 5 when he complained of nasal stuffiness, a tight feeling in the throat, and slight lassitude. These symptoms were still present on d + 6, when there was also a slight increase of nasal exudate. On d + 7 the quantity of nasal exudate had returned to the volunteer's normal amount. There was now some definite left-sided nasal obstruction and the voice had a nasal intonation. The throat felt sore, the fauces appeared slightly reddened, and there was slight cervical adenitis on the right side. This volunteer experienced no pyrexia, but it is noteworthy that until d + 5 his mouth temperature had not risen above 97·6°F, but on d + 5 and d + 6 it remained at 98·6°F. On the morning of departure (d + 8) his general condition was good and the throat appeared normal, but there was still some nasal obstruction and slight cervical adenitis. The nasal obstruction persisted for one day after leaving the hospital.

None of the volunteers developed symptoms suggestive of respiratory infection during the fortnight which followed their stay in the hospital.

Laboratory Findings

Virus identified as A.P.C type 1 was recovered from four of the volunteers (C, F, J, and L) and none from the remaining seven. Garglings collected on d + 2 were all virus-negative. Garglings from two volunteers (F and J) were virus positive on d + 4 and from three volunteers (C, J, and L) on d + 6. Two of the volunteers (J and L), from both of whom virus was isolated, showed clinical evidence of respiratory infection, which was more pronounced in volunteer J from whom virus was isolated on two consecutive occasions.

Table I relates these findings to the levels of type-1 A.P.C. antibodies in the volunteers' sera. Specimens of blood taken before administration of the culture-material showed a titre of type-1 neutralising antibodies of less than 20 in the four volunteers from whom virus was subsequently recovered and of 40 or more in the remainder. Complement-fixing antibodies were present in the pre-administration sera from all except one (volunteer L). Comparison of the pre- and post-administration sera showed, in the virus-positive group, a rise of twofold or more in both neutralising and complement-fixing type-1 antibodies. In the virus-negative group there were no significant rises in complement-fixing antibodies, but type-1 neutralising antibodies increased in three (volunteers B, D, and K). Post-administration serum from one volunteer (A) in the virus-negative group was not available for testing.

TABLE I—VOLUNTEERS TO WHOM A.P.C. TYPE 1 WAS ADMINISTERED, SHOWING RESPIRATORY SYMPTOMS, VIRUS RECOVERY, AND TYPE-1-ANTIBODY LEVELS IN PRE- AND POST-ADMINISTRATION SERA.

Volunteer	Respiratory symptoms	Virus recovery (days after administration)			Antibodies for A.P.C. type 1			
					Serum neutralisation *		Complement-fixation *	
		2nd	4th	6th	Pre	Post	Pre	Post
A	Nil	Neg.	Neg.	Neg.	640	n.d.	20	n.d.
B	Nil	Neg.	Neg.	Neg.	160	320	20	20
C	Nil	Neg.	Neg.	Pos.	< 20	40	20	40
D	Nil	Neg.	Neg.	Neg.	320	> 1280	20	20
E	Nil	Neg.	Neg.	Neg.	320	320	20	20
F	Nil	Neg.	Pos.	Neg.	< 20	80	10	30
G	Trivial	Neg.	Neg.	Neg.	320	320	20	20
H	Trivial	Neg.	Neg.	Neg.	320	320	15	15
J	Pyrexia, sore throat, cervical adenitis	Neg.	Pos.	Pos.	< 20	40	10	80
K	Trivial	Neg.	Neg.	Neg.	40	320	20	30
L	Nasal obstruction, sore throat, cervical adenitis	Neg.	Neg.	Pos.	< 20	160	< 5	240

* Titres are expressed as the reciprocal of the highest serum dilution showing complete neutralisation or 50 % complement-fixation. n.d. = not done.

The paired sera were also tested for neutralising and complement-fixing antibodies for A.P.C. viruses types 2–6. The results of the tests, with all 6 types, are shown in tables II and III.

Table II shows the findings in the group of volunteers from whom A.P.C. virus type 1 was recovered after administration. Increases of complement-fixing antibodies were observed for all 6 types, with the single exception of type-4 antibodies in the case of volunteer C.

TABLE II—ANTIBODY TITRES IN PRE- AND POST-ADMINISTRATION SERA OF VOLUNTEERS FROM WHOM VIRUS WAS RECOVERED

Volunteer	Date (1955)	Neutralising antibodies*						Complement-fixing antibodies *					
		Type 1	Type 2	Type 3	Type 4	Type 5	Type 6	Type 1	Type 2	Type 3	Type 4	Type 5	Type 6
C	May 11 ..	< 20	< 20	80	> 1280	320	< 20	20	10	20	40	20	30
	June 7 ..	40	< 20	80	> 1280	640	80	40	40	40	40	60	60
F	May 11 ..	< 20	1280	< 20	80	n.d.	n.d.	10	10	5	5	5	5
	June 6 ..	80	> 2560	< 20	160	n.d.	n.d.	30	30	15	30	30	30
J	May 11 ..	< 20	< 25	50	100	200	n.d.	10	5	15	20	10	5
	w.e. June 11	40	50	50	400	800	n.d.	80	80	80	160	80	80
L	June 11 ..	< 20	160	< 20	80	20	< 20	< 5	< 5	< 5	< 5	< 5	< 5
	June 13 ..	160	> 1280	80	> 1280	640	160	240	240	160	120	120	120

* Titres are expressed as the reciprocal of the highest serum dilution showing complete neutralisation or 50 % complement-fixation. n.d. = not done. w.e. = week ended.

In most instances the increases, in the same individual, were of similar magnitude for all types. They were greatest in the two volunteers (J and L) who developed clinical symptoms. Changes in the level of neutralising antibodies were more variable. Heterotypic responses were, in some instances, similar to the homotypic response, but the magnitudes of the increases which were observed were less uniform than those revealed by complement-fixation tests. There were several examples of a rise in complement-fixing antibodies accompanied by no change in the level of the corresponding neutralising antibodies.

Table III shows the findings in the group of volunteers from whom no virus was recovered after administration. No significant change was observed in the level of complement-fixing antibodies for any of the 6 types. Neutralising-antibody titres against the homologous type increased fourfold or more in two cases (volunteers D and K). In one instance (volunteer K) there was a heterotypic response of similar magnitude. Slight rises were observed in a third case (volunteer B). The remaining three volunteers showed no change in the neutralising-antibody levels.

Nose and throat swabs, which were taken from each volunteer before administration of the virus, were examined for the presence of hæmolytic streptococci, with a negative result in every case.

The swabs which were subsequently taken from the volunteers who developed clinical symptoms yielded, in the case of volunteer L, no hæmolytic streptococci and in the case of volunteer J, a light growth of hæmolytic streptococci which did not belong to group A.

Discussion

The present investigation provided both clinical and laboratory evidence of human infection by type-1 A.P.C. virus. Signs of acute pharyngitis, which were observed in two of our eleven volunteers, began on the fourth and fifth days after nasal instillation of the virus-culture material. The incubation period corresponded to that of " acute respiratory disease " (Dingle et al. 1954) and of " pharyngoconjunctival fever " (Bell et al. 1955). Neither of our two patients showed signs of conjunctivitis, but in other respects their symptoms resembled those of pharyngoconjunctival fever.

Virus was first recovered from these two cases on the fourth and sixth days respectively. Virus was also recovered, after similar periods had elapsed, from two volunteers who showed no clinical signs of infection. In all four of these volunteers no type-1 neutralising antibodies could be detected in the sera taken before the virus was administered. Subsequent specimens of sera showed in every case a distinct increase in type-1 neutralising antibodies. The occurrence in the same volunteers of heterotypic neutralising-antibody responses indicated that the serological tests alone were insufficient to establish the identity of the infecting virus type. These heterotypic responses reached higher levels than those observed in the cases recorded by Rowe et al. (1955). The explanation for this may lie in differences of technique or in peculiarities of the virus strains studied.

In three of the four volunteers from whom virus was recovered complement-fixing antibodies for type-1 virus were present in the pre-administration sera although neutralising antibodies for this type were absent. The subsequent increases which were observed in the level of complement-fixing antibodies constituted further evidence for A.P.C. infection in all four of these volunteers, but gave no indication of the identity of the infecting type.

TABLE III—ANTIBODY TITRES IN PRE- AND POST-ADMINISTRATION SERA OF VOLUNTEERS FROM WHOM VIRUS WAS NOT RECOVERED

Volunteer	Date (1955)	Neutralising antibodies *						Complement-fixing antibodies *					
		Type 1	Type 2	Type 3	Type 4	Type 5	Type 6	Type 1	Type 2	Type 3	Type 4	Type 5	Type 6
B	May 11 ..	160	< 20	20	320	80	40	20	40	15	20	20	20
	June 7 ..	320	< 20	20	640	80	80	20	40	15	20	20	20
D	May 11 ..	320	n.d.	< 20	< 20	n.d.	n.d.	20	5	10	10	10	10
	June 16 ..	> 1280	n.d.	< 20	< 20	n.d.	n.d.	20	5	10	5	10	5
E	May 12 ..	320	40	< 20	80	< 20	40	20	20	10	10	10	10
	June 8 ..	320	40	< 20	80	< 20	40	20	20	10	10	10	5
G	May 12 ..	320	80	80	160	< 20	n.d.	20	10	< 5	10	5	10
	w.e. June 11	320	80	80	160	< 20	n.d.	20	10	< 5	10	10	10
H	May 11 ..	320	> 1280	20	< 20	< 20	n.d.	15	15	10	15	15	15
	w.e. June 11	320	> 1280	20	< 40	< 40	n.d.	15	15	10	15	15	15
K	May 11 ..	40	< 20	< 20	20	160	< 20	20	30	20	20	20	20
	June 7 ..	320	< 20	< 20	160	160	< 20	30	40	20	20	20	30

* Titres are expressed as the reciprocal of the highest serum dilution showing complete neutralisation or 50 % complement-fixation. n.d. = not done. w.e. = week ended.

The seven volunteers from whom no virus was recovered all had type-1 neutralising antibodies in their pre-administration sera. No significant change in the level of complement-fixing antibodies was observed, and the only indications that infection might have occurred were the increases of neutralising antibodies in three of the cases.

Ginsberg et al. (1955) have suggested certain criteria for establishing the ætiological relationship of a new agent to a clinical disease. These criteria may be summarised as follows: (1) the isolation of the agent from patients with the disease; (2) the development of specific antibodies in relation to infection; (3) the correlation of susceptibility to infection with the pre-existing level of specific neutralising antibodies. The findings in the present investigation fulfilled all these criteria and provided evidence of an ætiological relationship between infection with type-1 A.P.C. virus and a respiratory illness, which in our cases could best be described as acute pharyngitis.

This virus type has been isolated by previous investigators from human adenoid and tonsillar tissues, but its potential pathogenicity has not hitherto been recorded.

Summary

A strain of A.P.C. virus type 1 was administered by nasal instillation to eleven volunteers.

Garglings taken on the second, fourth, and sixth days after the instillation were examined for the presence of type-1 virus, which was recovered from none of the volunteers on the second day and from four of them on the fourth or sixth day. Two of the volunteers from whom the virus was recovered developed acute pharyngitis on the fourth and fifth days. The remaining volunteers showed no clinical evidence of infection.

Paired sera were tested for neutralising and complement-fixing antibodies for A.P.C. viruses types 1–6. Neutralising antibodies for type-1 virus were not detected in the pre-administration sera of any of the four volunteers from whom the virus was subsequently recovered, but were present to varying titres in the pre-administration sera of the remainder. The virus-positive group all showed definite increases in neutralising antibodies for the homologous type and variable responses to the heterologous types. Three volunteers from whom no virus was isolated showed increases in neutralising antibodies.

Rises in complement-fixing antibodies were observed only in the group of volunteers from whom virus was recovered and were greatest in the two volunteers who showed clinical evidence of infection.

We wish to thank Dr. C. H. Andrewes for his advice and encouragement throughout this investigation; Dr. A. C. R. Wakeman for the radiological examinations; Dr. M. S. Pereira for the bacteriological examinations; and all the doctors who kindly sent us blood specimens.

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INJURY TO RECTUM AND ANAL CANAL BY ENEMA SYRINGES

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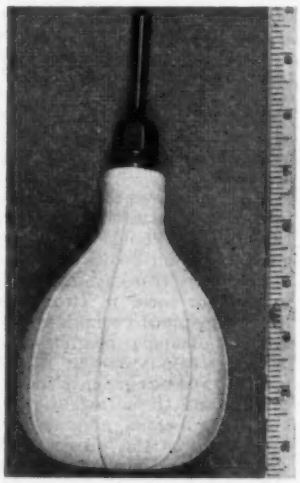
THE rectum and anal canal may often be injured by enema syringes but usually so slightly that no serious or annoying complications follow. Slight injuries would either heal spontaneously or be followed by abscess, fissure, or fistula, which may not be attributed to the real cause. For these reasons only the more dramatic injuries are reported and the great majority of injuries remain unrecognised or at least unreported.

In most cases errors of technique and unsuitable instruments seem to be the principal factors in producing such injuries. We have been able to find only 31 cases of injury by enema syringes published in English. These are summarised here, and an additional one is described. We exclude injury due to scalding or to corrosive fluids and to perforation of the colon either by enemas or colostomy washout; but we mention 1 case of injury to the colon because of its historical interest, being the first recorded case so far as we have been able to ascertain.



The instrument used by the patient. The nozzle is of bakelite, the capacity of the rubber bulb is 200 ml., and sharp compression of the bulb expels the fluid under considerable pressure. The opening of the nozzle is at its tip, and the apparatus is clearly difficult and dangerous to use. (Scale in inches.)

Case-report

A European male, aged 36, awoke on Aug. 13, 1955, feeling ill and apparently suffering from influenza. He decided that he would derive benefit from an enema, and for this purpose he borrowed a syringe (see figure) from a neighbour. He inserted the hard unlubricated 'Bakelite' nozzle, with some difficulty, at 10.30 A.M. and, there being no result, repeated the injection at 11.15 A.M. and again at noon. On each occasion, unaided by any other person, he used one bulbful of soap and water and squeezed the bulb firmly to empty it rapidly. There was no evacuation of the bowel, but rectal fullness was noticed soon after the first injection of fluid. At about 11 A.M. lower abdominal colic began, mild at first and gradually becoming more severe, and was succeeded a few hours later by continuous abdominal pain, with exacerbations on the slightest movement. At about 1 P.M. severe continuous pain developed over the sacrum and continued with increasing intensity, with no relief except by an opiate. At no time was there any complaint of anal pain or of the passage of blood per anum.

On examination at 3.15 P.M. he appeared ill, in great pain, with a temperature of 100°F, pulse-rate 104, and a dry furred tongue. Examination of the abdomen showed restricted respiratory movements, slight distension, severe lower abdominal tenderness, and lower abdominal rigidity. Bowel sounds were absent. Inspection of the anus revealed no bruising, laceration, or bleeding, but on digital examination the rectal wall, as high as the finger could reach, was grossly swollen and spongy and crepitated like subcutaneous surgical emphysema. No laceration was felt, but there was a little fresh blood on the

finger-stall. No sigmoidoscopy was done, for fear of aggravating what appeared to be extensive stripping of the rectal mucosa with peritonitis. Deep palpation on each side of the anus did not show any induration or tenderness which might suggest injury of the ischiorectal fossa or of the perianal tissues.

At laparotomy under general anæsthesia at 4 P.M. the peritoneal cavity was found to contain a little turbid fluid with flakes of fibrin. Careful search revealed no perforation of the rectum, pelvic colon, or any other hollow viscus into the peritoneal cavity. The entire rectum, as high as the pelvirectal junction, was grossly œdematous, bright red, spongy, and crepitant to the touch, but no gas-bubbles were seen through the peritoneal covering. There were no signs of bruising, induration, or swelling in the perirectal extraperitoneal cellular tissues, and it was therefore concluded that the injury was confined to the rectum, and that the entire rectal wall had been stripped. It was feared that such extensive stripping with highly irritant fluid might lead to sloughing of the rectum or to a stricture. Therefore a left iliac-loop colostomy was established immediately. The pelvis was not drained.

Postoperative progress was good. The patient was treated with intravenous fluids and gastric suction for four days, at the end of which time bowel sounds had returned and the colostomy worked for the first time. For five days he was given injections of penicillin and streptomycin. During this period the anus, anal canal, and rectum were examined daily to detect the development of rectal sloughing or of a local abscess at an early stage, but no such complication arose. Proctoscopy, first done five days after the injury, showed that the rectal wall was œdematous and red, but no breach of the mucosa was found. At this stage there was no trace of the gas-bubbles which had previously produced such marked crepitations. Sigmoidoscopy two days later showed that the rectum was much less œdematous but still red. Further sigmoidoscopy on the thirteenth day showed that the mucosa was of normal colour, very slightly œdematous, and with no signs of sloughing or of early stricture. Subsequently the colostomy was closed by resection and intraperitoneal suture. The further course was uneventful apart from the leakage of a little gas from the wound for less than twenty-four hours. Two months after the injury sigmoidoscopy to 11 inches showed a normal mucosa, with no apparent scarring or stricture.

Follow-up.—The patient has moved to another city, but we have heard that he suffers no ill effects six months after the operation.

Comments.—The bakelite nozzle of the enema syringe probably penetrated the rectal mucosa, possibly after the mucosa had been sucked into the terminal opening of the nozzle. The nozzle was rigid, and the patient acted with determination. Consideration of this type of instrument leads to the conclusion that excursions of the nozzle would be very difficult to control by a hand holding and forcefully squeezing the bulb, and that, in the course of the manipulations, it may readily have penetrated the rectal mucosa at a fold or a crypt. Then 200 ml. (the capacity of the bulb) of highly irritating fluid and air was forcefully injected, stripping the rectal mucosa. Since the rectal mucosa is relatively insensitive, it is difficult to say precisely which of the three attempts produced the damage, because it seems unlikely that all three did so. It was after the first attempt that rectal fullness was noted and before the second that abdominal colic began, and it seems most probable that the first was responsible. The symptoms and signs of peritonitis and the exudate found at operation are believed to have been the reaction to a severe injury of an organ with a peritoneal covering. Although the mucosal breach was neither felt nor seen, the injury was undoubtedly due to the nozzle, for it is impossible otherwise to explain the presence, within the rectal wall, of bubbles of gas.

Classification of Injuries

Ault (1939) suggested an anatomical basis for classifying such injuries according to the level of injury and the organ involved, and he suggested five main groups of cases. Since his proposed classification has some merit, we follow it here :

(1) Injury to the anus, anal canal, and structures below the levator ani muscle.
(2) Injury of the rectal mucosa—submucous perforation.
(3) Perforation into perirectal tissues above the levator ani muscle and below the peritoneum.
(4) Perforation into neighbouring viscera.
(5) Perforation into the peritoneal cavity.

Most of the published cases fall into one of these groups, but 2 of them cannot be classified, because there are not enough details, and in a few others it seems likely that several injuries were combined.

(1) There have been 4 cases of *injury to structures below the levator ani muscle.* In only 1 of them (Gabriel 1949) was the patient's age known (73) and information forthcoming about the nozzle, which was hard. In 3 (Rayner 1932) the enema was given by a trained nurse, the injury was visible at the anal margin, and the patients did not complain of pain until a week after the injury although all suffered a partial rectal slough. There were no deaths in this group. All the patients were males, and in each the enema nozzle was apparently thrust through the perianal skin.

(2) There have been 3 cases of submucous perforation : 3 cases published by Ballon and Goldbloom (1941), Bendit (1945), and Pinnock (1937), and the present case. Of the 4 patients 3 were men aged 49, 58, and 36, and 1 was a girl aged 5 years. In 2 cases the enema had been given by a trained person, in the girl by the mother, and in 1 case by the patient himself. A mixture of soap and water was used in 2 cases ; and in all of them a hard nozzle of rubber, bone, or bakelite, with a bulb or Higginson syringe, was used. All the patients became seriously ill with perineal, abdominal, or sacral pain. Inflammatory masses were felt on rectal examination, and there was severe melæna in the case described by Bendit (1945). 3 patients recovered (1 after developing a rectal slough), but the 4th died five days later, of a cerebral catastrophe and a sloughing rectum, having refused operation (Pinnock 1937). A permanent colostomy was not required in any of the 3 survivors. Stripping of the rectal wall is clearly a dangerous condition in which colostomy should be done as early as possible.

(3) There were 12 cases of *perforation into perirectal tissues* (Ault 1939, Gabriel 1949, Jones 1949, Klein and Scarborough 1953, Murray 1937, Pinnock 1937, and Shaw 1923). In these the severity of injury was greatest and the death-rate highest. 5 of the patients died ; the rectum sloughed in 7, of whom 3 required a permanent colostomy. There were 6 males and 4 females (the sex was not stated in 2), but the sex ratio is insignificant in so small a group. The ages (stated in 8 cases) ranged from 45 to 75, with 1 patient in the fifth decade, 3 in the sixth, 2 in the seventh, and 2 in the eighth. In 3 cases the type of instrument is not stated, but in the remaining 9 it was a hard nozzle. One nozzle was 12 inches long. The fluid was administered under unnecessarily high pressure in at least 6 cases ; in 5 of these a syringe was used, and in the remaining 1 a can containing the fluid was raised 6 feet above the level of the patient's buttocks. Of 8 cases where the identity of the person who gave the enema is stated, a nurse was responsible in 5, a midwife in 1, and the patient in 2. In 1 case the enema was given during labour, and in another post-partum after suture of a tear. In both these cases (Murray 1937, Shaw 1923) a hard nozzle was used by a trained person, a point which emphasises the extreme care which should be exercised in such patients, in whom pelvic viscera may be temporarily excessively mobile and congested and normal anatomical relationships altered. Clinically, these patients had severe local and, in some, abdominal pain. The site of perforation in Ault's (1939) case was $2^1/_2$ inches above the anus ; in Jones's (1949) $^3/_4$ inch above the anal canal and in the left wall of the rectum ; in 1 (Gabriel 1949) in the posterior rectal wall

just above the anal canal; and in 1 (Gabriel 1949) within reach of the examining finger. 2 patients (Gabriel 1949, Murray 1937) were treated without colostomy or cæcostomy and both died with rectal sloughing, 1 with anaerobic infection and the other with pyæmia. 9 patients were treated by early establishment of a colostomy, and 3 of these died. The remaining patient had a colostomy established three weeks after the initial injury and later developed a rectal stricture, for which the colostomy was retained permanently. The rectum sloughed in 7 of this group, including 3 patients who died: 1 died eight days after drainage of a retrorectal abscess due to infection by anaerobes, and death was attributed to cardiac failure (Gabriel 1949); another had pyæmia (Murray 1937); and the 3rd developed cellulitis of the abdominal and thoracic walls (Jones 1949). An explanation must be sought for the high incidence of rectal sloughing in this group, and it seems likely that the intense inflammation of the perirectal cellular tissues leads to thrombosis of the superior rectal artery or its branches, and in cases of stripping of the rectum a similar intramural thrombosis may develop. The peritoneum appears to have acted as an effective barrier to the spread of infection, for, despite the severity of the injury, only 2 patients developed peritonitis: 1 twenty-four hours after injury and twelve hours after colostomy, the patient subsequently dying (Jones 1949); and the other as a complication of pelvic cellulitis (Gabriel 1949).

(4) There have been 2 cases of *perforation into neighbouring viscera* (Galbraith 1937, Siler and Bebb 1950). Both patients were females in the sixth decade. In 1 the enema was given by a nurse, the character of the instrument being unstated; and in the other by an untrained person using a bone nozzle and a Higginson syringe. Neither patient became acutely ill at an early stage. In 1 a rectovaginal fistula was found three weeks after the enema, and this was repaired after establishment of a temporary colostomy. The other patient developed a similar fistula with a complete rectal slough and survived with a permanent colostomy. These 2 cases differ from those discussed above in that a long interval elapsed between injury and treatment, and the effects on the pelvic cellular tissue must have been, at least in the first instance, localised. However, the 2nd of these cases may reasonably be regarded as an instance of a combined injury, thus explaining the complete sloughing of the rectum, even though this did not apparently take place until some weeks after the injury.

(5) There were 8 cases of *perforation into the peritoneal cavity* (Cooper 1953, Green cited by Gorsch 1939, King 1930, Klein and Scarborough 1953, Pratt and Jackman 1945). Of the 8 patients 3 were females and 2 males (the sex of the remaining 3 was not stated). The ages of 3 are given; they were in the seventh and eighth decades. In 3 cases a hard nozzle was used, no information being available in the remainder. The enema was administered by the patient in 2 cases, by a patient and a friend in another, and by a chiropractor in yet another. A mixture of soap and water was used on two occasions, and peroxide on another. Where details are given, the symptoms and signs appear to have been dramatic and so severe that treatment was early in most cases. 1 of these patients died seven days after the enema. Rectal stricture developed in both patients known to have had soap-and-water enemata, but the other cases are reported in such scanty detail that it is impossible to draw any firm conclusions. 2 of this group were treated by colostomy and suture of the laceration, and the others by suture alone or by suture combined with local drainage.

Consideration of the whole group of patients shows that 15 were male and 12 were female, and the ages ranged from 5 years to 74: 1 patient was in the first decade, 1 in the fourth, 2 in the fifth, 5 in the sixth, 5 in the seventh, and 3 in the eighth. In 11 cases the enema was given by a trained person, and in 4 by an unskilled person; it was self-administered in 5. There were 8 deaths, and 4 of the survivors were left with permanent colostomies. In every case there was a severe prolonged illness involving at least one operation.

Injury to Colon

Although it is not strictly within the title of this paper, we describe briefly here the earliest published case of enema injury we found (Nugent 1832). For ritual ferocity the régime outlined must be unequalled.

A healthy newborn male, in accordance with the custom of the day, was given two doses of castor oil, the object being to get rid of all meconium. When this failed, calomel gr. 1 was given on the second day, to be followed an hour later by an enema given by a "nurse tender," the fluid being a mixture of turpentine and castor oil. This produced no result but a crying child and a little blood per rectum. The enema was therefore repeated, and an hour later the child was crying, in pain, and vomiting, and his abdomen was tender. He died four hours later, and necropsy revealed a perforation of the pelvic colon, 2 inches above the pelvirectal junction and about 7 mm. in diameter.

Behrend and Herrman (1933) and Kaufman et al. (1945) have described similar perforations of the pelvic colon by enema nozzles.

Treatment

Treatment of these injuries clearly depends on the circumstances peculiar to each, but certain principles have been enunciated and, in most instances, followed. Where intraperitoneal injury has been inflicted it is generally agreed that early laparotomy should be done, the fluid sucked out of the peritoneal cavity, the perforation sutured, possibly a drain left down to the site of the suture, and, where deemed necessary, the fæcal stream by-passed through a colostomy or a cæcostomy, which, to be effective, should be established without delay. It appears to be safe practice to establish a by-pass in most cases, because peristaltic movements of the colon are not gentle and may impose a great strain on a sutured perforation. Moreover an inkwell type of cæcostomy, established at the time of operation, would prevent gaseous distension, cause little inconvenience to the patient, and, on removal of the tube, close of its own accord.

Other factors—e.g., peritonitis and local abscess—require such treatment as the occasion demands. When consideration is given to injuries involving perirectal tissues, it is possible to advocate principles of treatment with greater emphasis. In view of the high incidence of rectal sloughing and its consequences, complete rest to the injured bowel appears to be essential and can only be achieved by colostomy or a well-functioning cæcostomy. These measures must be combined with local drainage of all affected areas, for which purpose it may be necessary to resect the coccyx. Although such measures may not prevent rectal sloughing, they will reduce the severity of its effects on the patient. General measures—e.g., intravenous feeding and blood-transfusion—may be required, and antibiotics have an important part to play. Where the rectal wall has been stripped, the available evidence indicates the establishment of a colostomy as early as possible, for sloughing took place in 2 patients (Bendit 1945, Pinnock 1937). Colostomy seems desirable as a temporary measure in those injuries which have caused a fistula into a neighbouring viscus, if attempted repair is to be successful.

For injuries below the levator ani muscle local treatment appears to suffice and consists in laying open and draining sinuses, fistulæ, and abscesses, and treating such specific infections as those due to gas-forming organisms.

Diagnosis of Injury

This may not always be easy in the absence of gross features, and assessment of the precise degree of injury

may be difficult because there may not be an early complaint by the patient, the rectal mucosa being relatively insensitive, especially in the elderly, and the depth of the injured part may lead to difficulty and delay in diagnosis. Bleeding is not a prominent early sign of injury and, at a later stage, may be due to the separation of sloughs. A perforation may be visible on proctoscopy or sigmoidoscopy; but, even when such examinations are possible, failure to see a perforation does not rule out its presence.

A barium enema is absolutely contra-indicated as a diagnostic measure. In 1 case (Klein and Scarborough 1953) it produced fibrosis and strangulation of the ureters, having leaked into the pelvic cellular tissues.

Production of Injury

The Patient.—The available evidence indicates that persons aged more than 50 are those likely to suffer such injury, possibly because of greater mobility of the rectal wall and the greater prevalence of local disease—e.g., prolapse and hæmorrhoids. At any age another ætiological factor is lack of knowledge of the angle made by the junction of the rectum and the anal canal and ignorance of the many crypts, valves, and folds in the normal rectum. The direction of the anal canal is towards the umbilicus, and a finger inserted before an enema tube will detect local disease. The perirectal tissues are loose and do not have a very rich blood-supply; they are therefore liable to constant reinfection with virulent organisms in the presence of a perforation, and by their anatomical position cannot achieve that degree of rest which is essential to the resolution of inflammation. Finally, the greater part of the rectum is devoid of a peritoneal covering, and its depth renders both diagnosis and surgical access difficult.

The Administrator of the Enema.—The second factor is the degree of skill of the person administering the enema. It is disturbing to note, from the foregoing account, how often a skilled person was responsible for the damage. Carelessness is therefore to blame, and as important as the exercise of care is the matter of taking heed of any complaint by the patient, and of desisting in the event of the least difficulty in the passage of the tube. The manipulations should always be conducted in a good light, and the tube should not reach beyond the rectum, a depth of 2 or 3 inches being sufficient. The terms "high enema" and "colonic lavage" are meaningless and seem to increase the danger to the patient pari passu with the enthusiasm of the attendant.

The Instruments and Solutions.—Hard nozzles and syringes should never be used, and it seems unnecessary that lethal weapons of the type shown in the accompanying figure should be on sale to the general public. It has been stated many times that the only safe equipment is a soft rubber tube with a side opening, well lubricated, and attached to a funnel held at a height of not more than 2 ft. above the level of the buttocks (Gabriel 1949). Ballon and Goldbloom (1941) suggested that the rectal mucosa might be sucked against a terminal opening and damaged—an accident which may readily happen with a bulb and nozzle. Bulbs and syringes involve the administration of fluid at uncontrolled pressures and at some risk. Bendit (1945) has pointed out that soapy solutions may contain an excess of potassium and sodium hydroxides, and that these may produce severe and fulminating infections. Plain water is a safe fluid and as effective as most.

Summary

A case is reported of injury to the rectal wall by a rigid nozzle and bulb used to give an enema.

31 other published cases have been collected and are reviewed.

The death-rate was high in this series; 8 out of 32 patients died.

4 other patients had permanent colostomies and all had a long and severe illness.

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PHTHALYLSULPHACETAMIDE AND NEOMYCIN IN THE TREATMENT OF INFANTILE GASTRO-ENTERITIS

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IF it is thought that an antibiotic might be useful in the treatment or in the prevention of epidemic infantile gastro-enteritis at this hospital, an attempt is made to assess its potential value by in-vitro sensitivity tests on intestinal pathogens, especially strains of the serological types of *Escherichia coli* isolated from the babies in the hospital; and, if possible, a clinical trial is conducted before the antibiotic is used to treat gastro-enteritides. Undoubtedly the best method of assessing the value of a drug is a controlled trial (Green 1954), but sometimes it is impossible to conduct one before it is expedient to use a new chemotherapeutic agent.

We describe here the assessment of two such substances; phthalylsulphacetamide by controlled trial, and neomycin without such a trial.

Phthalylsulphacetamide

Heineken and Seneca (1948) showed that phthalylsulphacetamide was concentrated in the intestinal mucosa of rabbits; but there is no easy method of proving whether this takes place, or is an advantage, in man. These workers used this drug in 28 cases of ulcerative colitis, of which 18 responded well, 9 moderately well, and 1 not at all.

Other workers had reported that phthalylsulphacetamide had cured cholera (Seneca and Henderson 1949) and typhoid fever (Wright 1949). These were such unusual claims for a sulphonamide that 2 of us took phthalylsulphacetamide 16 g. daily, the dosage recommended for treating cholera. This produced precipitant diarrhœa, tenesmus, and most embarrassing borborygmi. There was no alteration of the bacterial flora of the fæces,

TABLE I—RESULTS OF TRIAL TREATMENT WITH PHTHALYLSULPHACETAMIDE

Trial no.	No. of volunteers treated	No. of treated volunteers with symptoms				
		Stools		Borborygmi	Colic	Tenesmus
		Increased	Watery			
1	4	4	4	4	4	4
2	6	6	6	6	5	6
3	4	4	4	4	4	3
Total	14	14	14	14	13	13

Controls: none displayed any symptoms except that 2 had nausea, anorexia, and headache in the first trial.

in contradiction to the finding of Henderson and Seneca (1949) that after four or five days' treatment the stools of 3 of 4 healthy adults became sterile.

Since these unexpected results might have been due to the use of biased experimental subjects, they were fully reported to a group of medical students, some of whom were asked to volunteer for a further trial of phthalylsulphacetamide. The manufacturers provided control tablets made of excipient, which were the same size and shape as those containing the drug. 8 students were divided into two equal groups, but they were not told which group would receive the dummy tablets. Those who were given phthalylsulphacetamide developed the same symptoms as in the earlier experiment, but on completion of the experiment it was realised that each student had quickly detected which type of tablet he was receiving, the dummy tablets not having the slightly acrid smell of the phthalylsulphacetamide. This might have influenced the result; so the previous experiments were fully described to some more students, who were then asked to volunteer for a blind trial.

In this second trial the control tablets were placed in bottles containing cotton-wool to which a little powdered aspirin and acetic acid had been added; both types of tablets were then associated with the same smell. The students who were given dummy tablets had none of the symptoms experienced by those who took the sulphonamide.

Phthalylsulphacetamide later became available in a fluid mixture with kaolin and pectin which, it was claimed, eliminated any unpleasant side-effects; 1 of us (K. B. R.) took a three-day course of this new preparation, which produced no alteration in his fæcal flora and within twenty-four hours caused well-marked intestinal hurry. The makers suggested that the experimenter was at fault, and they supplied bottles of the excipient which looked and tasted exactly like their preparation of phthalylsulphacetamide.

All the previous results were reported to some students, 8 of whom volunteered for a blind trial. On the third day of treatment the fæces of 3 of the treated students showed a reduction in the number of *Esch. coli*, but the 4th student had sterile fæces. Nevertheless the treated students had the same gastro-intestinal upset as in all the previous experiments. The results of these trials are summarised in table I.

Blood-sulphonamide levels were estimated in some of us and our laboratory colleagues who took various courses of phthalylsulphacetamide. The results are shown in the accompanying figure. During the first trial the blood-sulphonamide levels were estimated daily in all the volunteers, so that they should have no indication about the type of tablet which each was receiving. The figure shows that there was very little sulphonamide in these students' blood. When 2 of us tried to repeat the experiment of Lehr (1949), taking 10 g. initially followed by four days' therapy with the same dosage as that given to the students, there was an unexpectedly high absorption, for which no explanation could be found.

Since phthalylsulphacetamide is 50% soluble in sodium bicarbonate (Poth and Ross 1944) it would be partially soluble in the alkaline intestinal contents; as a solution it could be absorbed into the mucosal cells, where, the pH being 7·1–7·4, the phthalylsulphacetamide would be precipitated within the cells. This could explain the findings of Heineken and Seneca (1948), who stated that phthalylsulphacetamide was not absorbed and that no appreciable quantities could be detected in the blood. The results shown in the figure do not agree with this last statement.

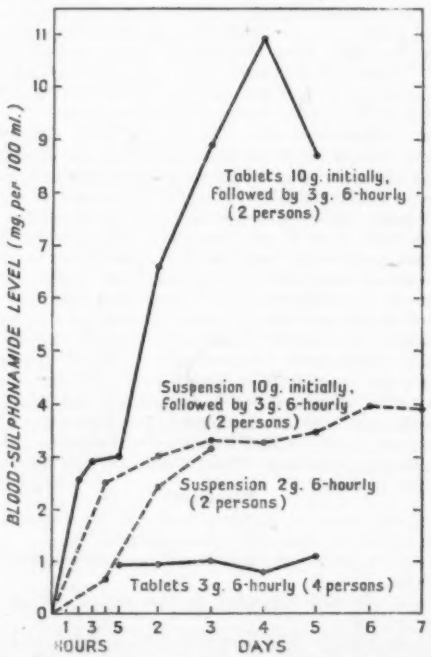
CONCLUSION

It was decided not to use phthalysulphacetamide for treating infantile gastro-enteritis because there was usually no appreciable reduction in the number of organisms in the fæces when it was given to healthy ambulant adults, in whom it caused a distressing disturbance of bowel function. Before the results of the trials were known, 4 babies, carriers of *Esch. coli* type O.111 (2 babies), *Shigella sonnei* (1 baby), and *Salmonella paratyphi-B* (1 baby), were each treated with the appropriate dosage of phthalylsulphacetamide; but after a full course of treatment none of these infants lost his pathogenic organisms.

Neomycin

Neomycin was first isolated at Rutger's University by Waksman and Lechevalier (1949). It is a water-soluble basic compound, most effective in an alkaline solution, and has a bactericidal action on many gram-positive and gram-negative bacteria but is ineffective against fungi (Waksman and Lechevalier 1949). It is toxic when given parenterally, causing auditory and renal damage (Waisbren and Spink 1950). This would preclude its administration by this route if it could be avoided, but these workers cured with very large oral doses an elderly woman with a chronic *Esch. coli* infection of the urinary tract.

Neomycin has been used topically as an ointment and as a solution in the treatment and the prophylaxis of septic conditions of the eyes and skin (Council on



Average blood-sulphonamide levels after oral phthalylsulphacetamide.

TABLE II—RESULTS OF NEOMYCIN THERAPY

Type of *Esch. coli*	Age when given neomycin (mos.)	Duration of neomycin therapy (days)	Days to improvement	Days excreting		Bacteriological relapses		No. of cases			
				Before neomycin	After neomycin	Day of relapse	Total no.	Severe	Mild	Carrier	Total
O.111 ..	4·0 (*0·25–11·0*)	6·0 (*5–13*)	1·9 (*1–4*)	7·7 (*1–34*)	2·6 (*1–6*)	2, 3, 7	3	5	13	4	22
O.55 ..	4·1 (*1–18*)	4·9 (*5–7*)	1·9 (*1–3*)	3·1 (*1–15*)	2·5 (*1–7*)	2, 2, 5, 5, 6, 12, 22	7	3	19	8	30
O.26 ..	5·0 (*1–7*)	6·0 (*5–7*)	2·2 (*1–3*)	2·9 (*1–3*)	2·0 (*1–5*)	3, 4, 4 ..	3	0	5	3	8
O.128 ..	1·0 (*1–1*)	6·5 (*6–7*)	3·0	2·0 (*1–3*)	1·5 (*1–2*)		0	1	0	1	2
O.125 ..	4·2 (*0·5–9*)	5·7 (*4–8*)	2·0 (*1–3*)	3·6 (*1–20*)	2·2 (*1–6*)	7, 7, 10, 12, 14	5	0	21	15	36
O.114 ..	2·0	9·0	..	5·0	4·0	..	0	0	0	1	1
Unknown	5·5 (*5–6*)	5·5 (*5–6*)	2·5 (*2–3*)	..	*	..	..	0	2	0	2
All ..	4·0 (*0·25–18*)	5·7 (*4–13*)	2·0 (*1–4*)	4·3 (*1–34*)	2·4 (*1–7*)	..	18	9	60	32	101

* Fæces from both these babies grew streptococci only on 2nd day of treatment.
Numbers in parentheses are limits of figures from which average was calculated.

Pharmacy and Chemistry 1954) and in the chemoprophylaxis of burns (Lowbury 1955). It has proved valuable in suppressing intestinal organisms before operations on the colon and rectum (Poth 1953, Fog 1954, Rowlands and Scorer 1955) and has been successfully used to treat babies with epidemic infantile gastro-enteritis due to *Esch. coli*. Adult as well as infant carriers of these organisms have been cured of their carrier state (Wheeler and Wainerman 1954, Stulberg et al. 1954, 1955). A few children with shigellosis and with salmonellosis have also been treated with neomycin (Ponce de Leon 1955).

At the end of April, 1954, a supply of neomycin became available for routine sensitivity tests. All the recently isolated pathogenic strains of *Esch. coli* were found to be fully sensitive to neomycin. The results of these tests agree with those of Gorzynski and Neter (1953).

The strains of *Esch. coli* excreted by babies in different epidemics of infantile gastro-enteritis have no predictable sensitivity to antibiotics and sulphonamides (Williams and Rogers 1954). At the beginning of June, 1954, strains of *Esch. coli* type O.111 were isolated which were insensitive to chloramphenicol, aureomycin, oxytetracycline, sulphadiazine, sulphathiazole, sulphadimidine, and sulphamerazine. These organisms infected the babies in one ward of the Parsons block, and several of the excreters of it developed severe gastro-enteritis, for the effective treatment of which an antibiotic was required.

Our in-vitro testing had shown that neomycin was the only antibiotic that was likely to be of value; and, when the first limited supply of neomycin was made available, only the severely ill babies were treated. Later it was possible to use the neomycin to treat mild cases and for chemoprophylaxis of carriers. In addition one of us (K. B. R.) took a five-day course of neomycin 100 mg. per kg. of body-weight, and his fæces became sterile on the third day of the treatment. There was no colic or tenesmus, but the neomycin caused a slight softness and increase in the number of stools.

DOSAGE

The neomycin was made up as a fluid mixture, each ounce of which contained neomycin sulphate 300 mg. (equivalent to 210 mg. of base) and kaolin 5·83 g. suspended in methyl cellulose. In all the cases the dosage was 20 mg. of the sulphate per lb. of body-weight daily. This dosage was nearly the same as that of Wheeler and Wainerman (1954), who gave 50 mg. per kg. of body-weight. Stulberg et al. (1954, 1955) sometimes used the same dosage but later they used 100 mg. per kg. of body-weight. The duration of treatment averaged 5·7 days, and varied between 4 and 13 days.

The urine of some of the babies treated with neomycin was examined, and blood-counts were made, at intervals of a few days. No albumin, casts, or red cells were found in any of the urine. The alterations found in the white-cell count were only those which any gastro-enteritides would show: the babies with severe gastro-enteritis showed polymorph leucocytosis, followed by postinfective lymphocytosis and a subsequent return to the normal relative lymphocytosis of babies. There were no alterations in the hæmoglobin levels. No skin eruption, untoward reaction, or any evidence of clinical moniliasis, developed in any baby receiving neomycin.

TRIAL

In 1952 a scheme was introduced at this hospital to eliminate epidemic infantile gastro-enteritis by excluding all excreters of pathogenic *Esch. coli* from the Parsons-block (infants') wards. The introduction of this scheme was followed by a reduction of hospital gastro-enteritis, but the incidence of infantile gastro-enteritis also decreased throughout Birmingham. So, when the epidemic due to the unusually resistant strains of *Esch. coli* type O.111 was over, there were relatively few cases of gastro-enteritis in the hospital. The other babies who were treated with neomycin were admitted to the hospital at irregular intervals in the next fourteen months.

The only period when it might have been worth conducting a controlled trial was when babies in one of the Parsons-block wards began to excrete *Esch. coli* type O.125. Probably many of those excreters would never have developed gastro-enteritis, but some of the babies were still very ill from the disease for which they had been admitted. In a properly conducted controlled trial the cases should be allotted in strict rotation to the treated and control groups; and, if all these ill babies had been placed in the treated group, it would have made it very difficult to assess the result of a trial.

Results

It was soon apparent that neomycin therapy was associated both with a very early cessation of gastro-enteritis and a rapid disappearance of the specific serotype from the fæces, and with the lack of development of enteritis if treatment was started early. Since we examine the fæces of the babies at short intervals if a carrier is found in a ward, many of the infants treated later in the series were only mildly ill, or merely carriers, when neomycin therapy was begun. The results of neomycin therapy are summarised in table II.

The classification into mild and severe gastro-enteritis was the same as that defined by the Medical Research Council (1953). All the babies who were ill responded well to neomycin therapy, and none of the 60 mildly affected babies treated with neomycin deteriorated.

TABLE III—4 FATAL CASES TREATED WITH NEOMYCIN

Case no.	Age when neomycin started	Days of therapy	Days to improvement	*Esch. coli* type	Days excreting		Severity of gastro-enteritis	Previous therapy	Necropsy findings
					Before therapy	After therapy			
1	2 mos.	8	1	E.2581	35	8 (never lost E.2581)	Severe	..	Bilateral staphylococcal pyothorax and suppurative bronchopneumonia
2	6 mos.	8	Never	O.111	1	9 (never lost O.111)	Ileostomy	..	Chronic interstitial focal nephritis, peritonitis
3	2 mos.	6	1	O.111	16	6 (never lost O.111)	Mild	Sulphadiazine and aureomycin	Fallot's tetrad of heart; acute purulent leptomeningitis
4	1 week	1/2	Never	None	..	..	Severe	Oral penicillin	In hospital 16 hr.; bilateral subdural hæmatoma

The histories of the 4 babies who died while on neomycin therapy are summarised in table III.

The 1st baby who died had a pyogenic infection which undoubtedly contributed to its death, and the staphylococci isolated from a bronchus and the pleural cavity were both fully sensitive to neomycin. Waisbren (1956) stated that blood-neomycin levels of 1 μg. per ml. could be demonstrated after oral administration. Poth (1953) noted that 3% of an oral dose could be recovered from the urine although only slight antibacterial activity could be shown in the blood. It was obvious that the absorption of neomycin was not sufficient to have affected the infection in this baby.

The 2nd baby who died was in extremis after many attacks of intestinal obstruction, for which three laparotomies and an ileostomy had been done. Although this baby's urine was not examined before and after the neomycin therapy, it was not thought that the neomycin had contributed to the chronic interstitial nephritis found post mortem.

In the 3rd baby who died, oral neomycin therapy failed to prevent the onset of meningitis.

The 4th baby who died had developed diarrhœa in a neighbouring maternity hospital, where he had had three days' intravenous therapy. Diarrhœa was still present when the infant was admitted to this hospital in a dehydrated and collapsed condition. Only three doses of neomycin were given before the baby died. No potentially pathogenic organism was found in the fæces during life or from specimens taken post mortem. No other baby developed enteritis at the maternity hospital where this baby had had diarrhœa for three days; so it is very unlikely that this infant's enteritis was caused by a pathogenic *Esch. coli*.

An unexplained finding among the first 3 of these babies who died was the failure of neomycin to eliminate the pathogenic *Esch. coli* from their fæces. This did not happen in any baby who lived.

9 children infected with *Sh. sonnei* were treated with neomycin. None was seriously ill, and most of them were treated as outpatients, which made it difficult to culture their fæces at regular intervals and very difficult to follow the infants for long after therapy had ceased. All made a rapid clinical recovery. 7 ceased to excrete *Sh. sonnei* in an average of four days; 1 continued to excrete *Sh. sonnei* after a course of seven days, and 1 relapsed two days after the cessation of neomycin therapy. 3 of these children had been previously treated with sulphonamides, and 1 with tetracycline, which had not eliminated *Sh. sonnei*. The fæces of 2 of these infants were cultured every day but grew no *Esch. coli* after two days' therapy; on the third and fourth days MacConkey plate cultures gave a pure growth of *Sh. sonnei*; and two days later the fæces of these 2 infants were sterile. Many of the later specimens from the treated children grew only *Sh. sonnei* from the subcultures made after selenite enrichment (Rogers 1954a). The only *Sh. alkalescens* infection was in a case of chronic diarrhœa of many months' duration. After neomycin therapy and the disappearance of *Sh. alkalescens* the diarrhœa ceased, and had not recurred six months later.

There was no clearance of the salmonella from the fæces of 2 infants who were carriers of *Salm. johannesburg*, both of whom were given neomycin and oral streptomycin. These babies had continued to excrete the salmonella after their acute infections had been treated with chloramphenicol. In-vitro tests had shown that the strains of salmonella isolated after chloramphenicol treatment were fully sensitive to chloramphenicol, streptomycin, and neomycin. A baby, aged 5 months, who was a carrier of *Salm. typhimurium* had a bacteriological relapse two days after the completion of a six-day course of neomycin.

Bacteriological Methods

When babies were being treated with neomycin, their fæces were examined daily and for five days after the cessation of treatment; if they were in hospital at the end of that time, the fæces were cultured twice a week; and, if the babies attended the outpatient department, fæcal specimens were obtained for culture.

The colonies on MacConkey plate cultures were examined by slide agglutination to exclude the pathogenic serological types of *Esch. coli*, and every new strain was confirmed by tube agglutination. If any infant had loose motions, the fæces were examined for salmonellæ, shigellæ, and *Giardia lamblia* (Rogers 1954a).

As mentioned earlier, if a carrier of a pathogenic serotype was found in a ward, the fæces of all the contacts were examined at short intervals—if possible, every day.

No special cultures were made to isolate candida nor were records kept of the number of times they were found; but a considerable number of specimens grew candida when the coliforms disappeared under neomycin therapy.

In-vitro sensitivity tests were made by a modified ditch-plate diffusion technique, on boiled blood media, when every new strain of *Esch. coli* isolated was compared with the same standard. Strains isolated from the babies receiving neomycin, either during or after therapy, were examined by the same method. There was no evidence of any resistance developing at any time during these tests—a finding similar to that of Stulberg et al. (1955).

Since neomycin became available for in-vitro testing in April, 1954, more than 400 strains of *Esch. coli* were examined; and none was found insensitive to neomycin. The first 400 strains examined were as follows: O.128 (12), O.126 (18), O.125 (84), O.119 (2), O.114 (6), O.111 (93), O.55 (81), O.26 (85), E.2581 (18), and O.28 (1). These figures do not include strains found in the fæces of a baby under treatment or with a bacteriological relapse.

83 strains of *Sh. sonnei* have all been fully sensitive to neomycin, as have 7 strains of *Salm. typhimurium*, 3 of *Salm. pullorum*, and 2 of *Salm. johannesburg*.

Discussion

Wheeler and Wainerman (1954) treated with neomycin 14 babies with gastro-enteritis due to *Esch. coli* type O.111; the epidemic strain was resistant to chloramphenicol, which had previously produced satisfactory clinical and bacteriological results. After four days' neomycin therapy *Esch. coli* type O.111 disappeared from the fæces of all the babies. There were one bacteriological

and one clinical relapse. No strains resistant to neomycin appeared during these studies. Adult carriers of *Esch. coli* type O.111 ceased to excrete these coliforms after treatment with neomycin 100 mg. per kg. of body-weight.

Stulberg et al. (1954) successfully treated with neomycin 23 premature babies with epidemic gastro-enteritis due to *Esch. coli* type O.111. These babies had not improved on aureomycin therapy, and in-vitro sensitivity tests later showed that the epidemic strain was insensitive to streptomycin and to aureomycin. Twenty-three attacks of enteritis were treated in 21 babies: 2 infants had a second attack of enteritis, and 1 developed enteritis, when *Esch. coli* type O.111 reappeared in its fæces after the earlier clearance of a carrier state of the same organism. There were thirteen bacteriological relapses in the 21 infants treated.

Stulberg et al. (1955) described how neomycin was effective in the treatment of premature babies with epidemic gastro-enteritis due to *Esch. coli* O.127. This epidemic lasted more than four months and involved 60 babies. Neomycin was also used to treat the carriers of the epidemic strain.

The satisfactory clinical response we obtained with neomycin in epidemic infantile gastro-enteritis due to *Esch. coli* is in accord with previous reports. Our babies became clinically well in an average of two days and lost their strain of *Esch. coli* in an average of two and a half days (table II)—figures which are very like the times reported by Stulberg et al. (1954, 1955).

Neomycin was equally effective in the treatment of both carriers and of cases, and there was very little difference between the time of recovery of the mild and severe cases of enteritis (about two days each). No toxic effects were observed.

At this hospital vitamin K is given if a severe case of gastro-enteritis requires a prolonged course of intravenous alimentation. None of the 9 severely ill babies treated with neomycin was given vitamin K, because it was possible to stop the intravenous therapy soon after neomycin therapy was started. All the babies were given a preparation of vitamins A, B complex, C, and D.

5 babies who had bacteriological relapses (1 with *Esch. coli* type O.111, 1 with type O.55, and 3 with type O.125) were treated with second courses of neomycin, which eliminated the pathogenic strains of *Esch. coli* from their fæces.

Another carrier of *Esch. coli* type O.26 was successfully treated with neomycin, but a month later this infant had a mild attack of enteritis due to *Esch. coli* type O.55, which responded well to neomycin therapy. None of these 6 babies showed any ill effects during or after the second course of neomycin; nor was there any evidence of resistance developing among the strains isolated from these babies or from the 8 others with bacteriological relapses.

Fowler (1955) suggested that staphylococcal enteritis might develop in patients treated with neomycin, and postulated that staphylococcal enteritis was another example of cross-infection. There was no case of staphylococcal enteritis in the present series, but staphylococcal enteritis may occur among neomycin-treated patients when someone in their ward is a carrier of a neomycin-resistant epidemic strain of staphylococcus. Dr. E. Lowbury (personal communication) reports that no neomycin-resistant strains have appeared among the burns treated with topical neomycin. We have tested eight hundred and forty strains of staphylococci, and all were fully sensitive to neomycin. Four strains of staphylococci isolated in widely separated hospitals from fatal cases of staphylococcal enteritis, and four strains obtained from cases in a single epidemic at a fifth hospital, were all fully sensitive to neomycin; so possibly neomycin may be of value in the treatment of staphylococcal enteritis.

The administration of neomycin proved effective in the treatment of 17 babies whose gastro-enteritis had not been improved by previous therapy with sulphadiazine (9), succinylsulphathiazole (2), chloramphenicol (2), aureomycin (3), and oxytetracycline (1).

In-vitro testing had shown that the strains of *Esch. coli* from the 17 cases mentioned above were insensitive to the antibiotics which were clinically ineffective, and neomycin therapy produced both a clinical improvement and the disappearance of the pathogenic types of *Esch. coli* from the fæces of these babies.

The Council on Pharmacy and Chemistry (1954) stated that neomycin had a slight laxative effect. The neomycin sulphate used in the present study was in a mixture with kaolin and methyl cellulose, substances which might improve gastro-enteritis; so it is worth noting that 4 babies with enteritis had been given 'Kaopectate,' the vehicle of the neomycin mixture, for four, six, six, and ten days without any improvement in the diarrhœa, which ceased after one, two, two, and two days of subsequent neomycin therapy.

Ponce de Leon (1955) reported that neomycin was successful in the treatment of 12 babies and 3 older children with salmonellosis and 7 babies and 3 children with shigellosis. Most of the babies were cured clinically and bacteriologically, but 1 with typhoid and 3 with shigellosis were no better. Ponce de Leon reported no untoward effects due to the antibiotics. At this hospital a few infants with dysentery were treated with neomycin with uniformly good results; and 3 salmonella carriers were unsuccessfully treated with neomycin.

Bacteriological relapses after neomycin therapy were reported by Wheeler and Wainerman (1954) and Stulberg et al. (1954, 1955). Since cultural techniques are different in each centre, and the cases are followed for different periods after the completion of therapy, the relapse-rates of different workers are not comparable. Moreover, since the babies in many of the reported series were kept in wards in which there was an endemic infection with a single type of *Esch. coli*, some of these relapses might well be reinfections; but, since 2 of our infants who attended as outpatients had relapsed twelve and twenty-two days after leaving hospital, this is certainly not so in every instance.

One baby, nursed in a ward where *Esch. coli* type O.55 was endemic, had a bacteriological relapse as well as a second mild attack of gastro-enteritis, which responded well to a second course of therapy. This was the only baby who had a clinical relapse, but 18% of our babies had bacteriological relapses, a finding very like that of Stulberg et al. (1955). The bacteriological relapse-rate was comparable with that we have experienced after therapy with other antibiotics, but the clinical relapse-rate was much lower. The babies who had bacteriological relapses had been treated with neomycin for an average of five and a half days. The pathogenic type of *Esch. coli* disappeared after an average of two and a half days' treatment, and the fæces remained free from these coliforms for nine and a half days; the pathogenic type of coliforms reappeared in an average of six days (range from two to fifteen) after cessation of treatment. These findings show the importance of continual surveillance of babies who stay in hospital after treatment has been completed. None of our babies infected with a pathogenic type of coliform and treated with neomycin relapsed immediately after therapy ceased. One baby who relapsed after five days' treatment received a further course of neomycin lasting thirteen more days. He showed no ill effects after eighteen days' therapy.

Stulberg et al. (1955) reported such relapses, which they controlled by continuing neomycin therapy until the babies were discharged from hospital. Wheeler and Wainerman (1954) also maintained babies on neomycin therapy until they left hospital or for two or three weeks.

Since very little neomycin is absorbed from the intestines (Poth 1953, Waisbren 1956), it would probably be safe to continue neomycin therapy longer, and this might lower the relapse-rate. However, since so little neomycin is absorbed, parenteral infections must be treated with other antibiotics (Wheeler and Wainerman 1954). This was well illustrated by our 1st fatal case (see above).

Todd and Hall (1953) advocated chemoprophylaxis of carriers of the pathogenic serotypes of *Esch. coli*, and Stulberg et al. (1954) suggested that all excreters be treated until discharged from hospital. The more recent experiences of Stulberg et al. (1955) showed how neomycin prophylaxis among premature babies who had to be kept in hospital a long time eventually controlled an epidemic when it was not expedient to close this premature-baby unit. We consider that it is better to close and to fumigate an infant's ward if there has been an epidemic of *Esch. coli* enteritis (Rogers 1954b) because neomycin therapy, although it can effectively control the excretion of these serotypes, cannot eliminate them from the dust or from the furnishings.

Summary

The oral administration of *phthalylsulphacetamide* caused severe gastro-intestinal disturbances in healthy adults, had very little effect on intestinal organisms, and gave appreciable blood-sulphonamide levels. No case of gastro-enteritis was treated with phthalylsulphacetamide.

Neomycin seems to be a very valuable addition to the antibiotics which can be used in enteritis due to *Esch. coli*: babies treated with it gave a uniformly good clinical and bacteriological response, but there was an 18% bacteriological relapse-rate.

No mildly ill baby with gastro-enteritis became severely ill on neomycin therapy.

Since little neomycin is absorbed from the intestines, any parenteral infection must be treated with another antibiotic.

No strain of staphylococci insensitive to neomycin was found; the strains tested included eight isolated from staphylococcal enteritis. If an epidemic strain of staphylococcus were to become resistant to neomycin, staphylococcal enteritis could occur among cases treated with neomycin.

We thank many of the clinicians at the Children's Hospital, Birmingham, for treating their cases with neomycin; the students who so cheerfully submitted to the experiments; Dr. R. Gaddie for blood-sulphonamide estimations; and Dr. R. E. O. Williams for supplying the staphylococci isolated from cases of staphylococcal enteritis. Messrs. British Schering Ltd. and Messrs. Ward, Blenkinsop & Co., Ltd. supplied the phthalylsulphacetamide and the control tablets and mixtures; and Messrs. Upjohn supplied the neomycin.

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DEXTRAN WITHOUT REACTIONS

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IN a previous report (Wilkinson and Storey 1953) reactions were reported in each of five volunteers who had received 500–1000 ml. of 6% dextran in 0·9% saline solution by rapid intravenous infusion. These reactions were resolved into two components or phases; one was characterised by urticaria, coming on during the infusion or soon after this was completed and lasting for up to two hours, and the other by vasomotor disturbances which appeared after the infusion was completed. Very similar observations had been earlier reported by Heisto and Lund (1953), who also found that a reduction in plasma-volume accompanied or followed the urticarial phase of the reaction, which they concluded was allergic.

The serological activity of native dextran is well established (Hehre and Sugg 1950, Neill and Abrahams 1951, Kabat and Berg 1952), but there is also evidence that such activity varies for different types of dextran. Pulaski (1951) found that reactions occurred in 40% of American soldiers to whom he administered dextran solutions prepared in Britain or Sweden, but Amspacher and Artz (1951) did not observe any reactions after injecting a solution of dextran of American origin into similar subjects. This latter dextran was synthesised by a different strain of *Leuconostoc mesenteroides* (B512) from that used for either the Swedish or British dextran; the B512 strain produces a dextran molecule with a low degree of side-branching and fewer 1 : 3 linkages.

It has been suggested that reactions are due to the presence in the solutions infused of dextran of large molecular weight; this suggestion is supported to some extent by the observation of Hehre et al. (1952) that complement-fixation by dextran might occur at lower dilutions with high than with low molecular-weight dextran. Clinical dextran of British manufacture contains a higher proportion of large molecular dextran than either the Swedish or American solutions. Persistence of the effect of infused dextran on plasma-volume depends largely on the dextran of larger molecular weight. If, however, the presence of such material is liable to increase the tendency to reactions it should be removed from solutions for clinical use.

It also seemed possible that the urticarial phase of the reactions might be related to the structure of the dextran molecule, and so to the strain of polymerising organism, rather than to the size of the molecules which were injected. It was clearly desirable to find out whether a solution of B512 dextran, containing as much dextran of large molecular weight as the solutions used in our previous experiments, could be rapidly infused into healthy subjects without giving rise to reactions; a pilot experiment by F. Fletcher (personal communication 1953) showed that this preparation gave a very low incidence of reactions in a large number of healthy volunteers to each of whom 30 ml. was administered by intravenous injection.

The composition of the solutions used in the earlier experiments (batch 225) and the present experiments (batch 3556) is indicated by the intrinsic viscosities shown in fig. 1; batch 3556 contains rather more dextran of high molecular weight than batch 225.

Methods

The six volunteers were healthy fully grown males aged 21–26. The conditions of the experiments were similar to those previously described except that each subject received 1 litre of 6·0% dextran in 0·9% saline solution (batch 3556); the duration of the infusion

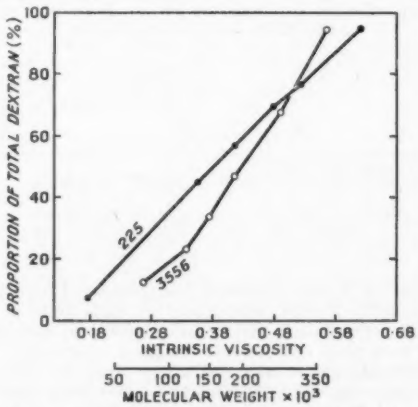

Fig. 1—Percentage composition of two dextran solutions in terms of intrinsic viscosity and molecular weight.

varied from 25 to 63 minutes, and the subjects remained in bed during and for 12 hours after the infusion. Packed-cell volume was measured as before and the subjects were closely observed during and after the infusions. The dextran levels in urine and serum were measured by the modified anthrone method of Bloom and Willcox (1951).

Results

Urticarial reactions did not ensue in any of the six volunteers. One did not experience any disturbance at any time, but each of the remaining five noticed some vasomotor disturbance. These five men all noticed fullness of the head: three while lying down (two soon after the infusion was completed, and one after several hours had elapsed); another only when he sat up; and the last man after getting out of bed 20 hours after the infusion. In two the fullness became a headache, which lasted 48 hours. In two subjects flushing of the skin and fullness of the superficial veins appeared soon after completion of the infusion and lasted several hours. Only one man experienced any severe disturbance on getting up the morning after the infusion. Three-quarters of an hour after having breakfast in bed and just after the second venepuncture of the day, he got out of bed and began to feel dizzy and have frontal headache and pain in the lumbar region; during the day he completely recovered. One vomited $2^1/_2$ hours after the end of the infusion and four times in the next $2^1/_2$ hours; each subject ate a three-course lunch either just before or just after the infusion was completed.

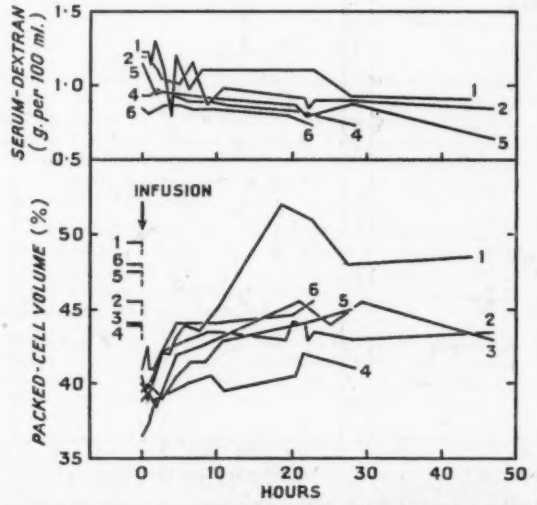

Fig. 2—Variations in packed-cell volume and serum-dextran level following the rapid infusion of 1 litre of 6% dextran in 0·9% saline.

Urinary Excretion of Dextran

Within 6 hours 11–14% and by 20 hours 16–18% of the dose of dextran had been excreted in the urine. In one subject, whose urinary dextran excretion was measured for 77 hours, only 2·4% of the dose was excreted between 26 and 77 hours after the infusion. The difference in urinary excretion between the present series and the previous one accords with the different molecular-weight composition of the solutions used.

Changes in the Blood

Changes in packed-cell volume and serum-dextran levels are shown in fig. 2. The initial sharp fall in packed cell-volume was followed in the next 6 hours by an increase of up to 5%, and in some instances this increase continued slowly. In only one volunteer was there a pronounced late change, which was associated with the only severe vasomotor disturbance that was observed. These observations are in contrast with those of the previous series in which the initial hæmodilution immediately after the completion of the infusion was followed by hæmoconcentration during the succeeding 6 hours, with a later slow fall in packed-cell volume to a low value again at the end of 24 hours.

Total red-cell volume was again calculated from the ideal weight for height and age, and from this red-cell volume and the change in packed-cell volume the change in plasma-volume immediately after the infusion of a litre of dextran solution was calculated. In the six volunteers it was 1144, 1100, 1045, 1000, 793, and 721 ml. The calculated increase bore no relation to the rate of infusion or body-weight; this increase amounted to 793 ml. after the most rapid infusion of a litre (in 25 minutes) into the smallest subject (65·4 kg.), and to 721 ml. after the slowest infusion (in 63 minutes) into the heaviest subject (76·3 kg.).

Discussion

The division of the reactions previously described into urticarial and vasomotor phases appears to be justified. No urticarial reactions occurred in the present series, but there were mild signs of circulatory overloading, and one subject experienced a vasomotor disturbance which symptomatically and in its effect on packed-cell volume resembled those previously described. Vasomotor disturbances were perhaps avoided by keeping the subjects in bed longer after the infusion; the increase in packed-cell volume during this period of recumbency suggests that there was a redistribution of the intravascular and interstitial components of the extracellular fluid with a gradual reduction in the excessive volume of intravascular fluid.

The solution (3556) used in these experiments contained dextran synthesised by a different strain (B512) of *L. mesenteroides* from that used in the previous experiments. The present solution also contained a larger proportion of material of the largest molecular weight. The absence of urticarial reactions after the rapid infusion of this solution under similar conditions to those in which another solution (225) caused reactions in every subject suggests that the solutions may have different antigenic properties in the man. This suggests that in the production of urticarial reactions the structure of the dextran molecule is more important than the presence of dextran of large molecular weight. This conclusion, if correct, is important, for it excludes one of the objections that have been raised to the inclusion of fractions of larger molecular weight in clinical dextran solutions. The duration of the effect of a solution of dextran on plasma-volume

depends mainly on the proportion of the dextran which is too large to be lost readily through even the unusually permeable capillaries of inflamed tissues, and which therefore is retained within the blood-vessels until it is taken up by the cells of the reticulo-endothelial system or is metabolised. Although large dextran molecules may have other undesirable effects it seems unlikely that their size is alone the cause of urticarial reactions in man.

Summary

A 6% solution of dextran, synthesised by the B512 strain of *L. mesenteroides*, in 0·9% saline solution was rapidly infused into six healthy volunteers. None of the volunteers showed any urticarial reaction, but five had vasomotor disturbances, which were severe in one and mild in four.

I am indebted to the volunteers who submitted to these experiments, to Mr. L. E. Martin for estimations of dextran, and to Bengers Laboratories Ltd. for a supply of the dextran solutions and for data regarding its composition.

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SIZE OF ADRENAL CORTEX IN EAST AFRICAN MALES

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THE size of an adrenal gland indicates its potential capacity for secretion. Therefore, if the average size of the adrenal cortex is reduced in a given population, this fact is significant, especially if the morphological and pathological patterns of that population are unusual, as they are in East Africans. For this reason the adrenal cortical and medullary masses in East African males were compared with those of North Americans of European extraction.

Method

24 fresh adrenal glands from East African males were examined. In every case death had been either very sudden (e.g., car accident or homicide) or caused by some condition unlikely to affect the mass of the adrenal glands (e.g., intracranial hæmorrhage or pneumonia). Each gland was dissected free from fat and connective tissue, and the adrenal vein was divided flush with the capsular surface. The gland was blotted dry, weighed in grammes to two places of decimals, and fixed in formol-saline solution. Serial paraffin sections, stained with hæmatoxylin and eosin and 10-μ thick, were examined at intervals of 2 mm. through the gland. Photographic enlargements (×10) were made of each section. The portions representing cortex and medulla in each photograph were then cut out and weighed separately. From their weights the cortico-medullary ratio was obtained. From this ratio and the weight of the fresh gland the weights of the cortex and of the medulla were calculated by simple proportion.

BODY-WEIGHTS AND WEIGHTS OF ADRENAL GLANDS IN EUROPEANS AND EAST AFRICANS

—	No.	Average combined weight of both adrenals (g.)	σ (g.)	Average body-weight (kg.)
European males (Roessle and Roulet 1932) ..	328	13·82	±2·80	53·10
East African males (Mulago Hospital) ..	45	9·13	±2·32	43·58

In one gland photographs taken at every 100 μ were used, and in another at every 1000 μ (1 mm.). In one case the end-result was identical with, and in the other 2% different from, that obtained by using sections at 2 mm. intervals.

Results

The mean total adrenal-gland weight was 3·8 g. (2·2–5·3 g.). The mean cortical weight was 3·2 g. (2·0–5·1 g.) and was in each case directly proportional to the total weight. The mean medullary weight was 0·51 g. (0·15–0·9 g.) and bore no relation to the total weight (fig. 1).

Discussion

Fig. 1 includes data calculated from the findings of Swinyard (1940) on the cortico-medullary ratio of the adrenal glands of North American whites and Negroes. The total-gland weights were heavier than in the East Africans (4·3–8·0 g. for whites and 2·7–6·1 g. for Negroes, male and female). The bottom of the North American

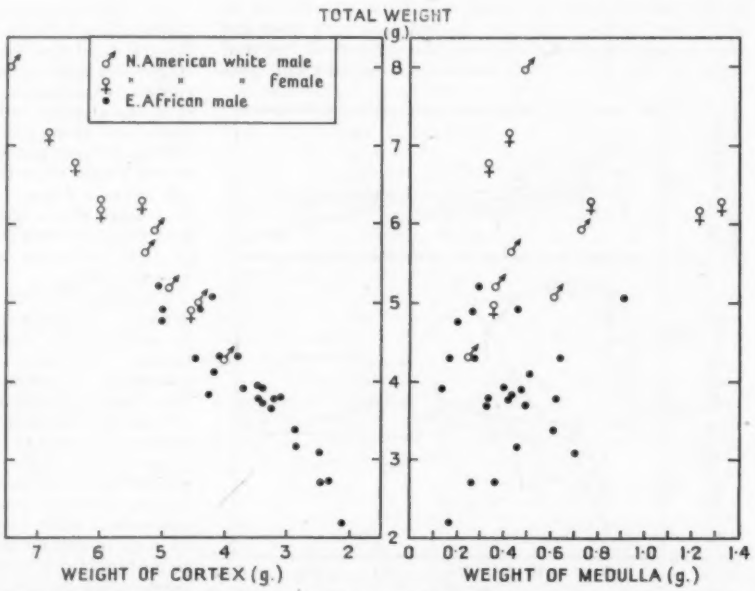

Fig. 1—Relations of weight of cortex and weight of medulla to weight of total adrenal gland in North American whites (data deduced from Swinyard 1940) and in East African males.

white range just reaches the top of the East African range. The cortical weights were much heavier in the North American whites but were still proportional to the total-gland weights. The medullary weights, however, were about the same in both series and bore no relation to total-gland weights.

Since these samples of populations are so small, the combined weights of both adrenal glands and the body-weights of 45 other East African males (collected at Mulago Hospital by Prof. J. N. P. Davies) are compared with those of 328 European males (Roessle and Roulet 1932) in the accompanying table. It will be seen that the adrenal glands are disproportionately smaller in the East Africans. That the combined weight of both adrenal glands is independent of the body-weight can be seen in additional data collected at Mulago Hospital (fig. 2).

It therefore appears certain that, in the East African males examined, (1) the smaller weight of the adrenal

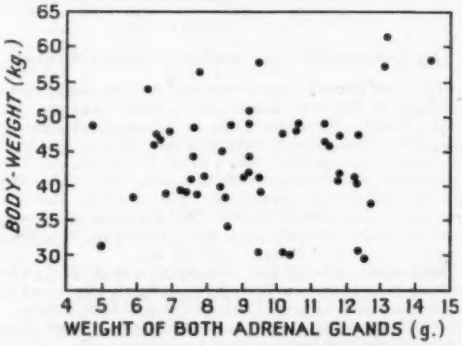

Fig. 2—Lack of correlation between body-weight and combined weight of both adrenal glands in East Africans.

glands is due to the smaller weight of the adrenal cortex, and (2) the weight of the cortex is largely independent of the body-weight.

These findings corroborate the suggestive biochemical studies of Barnicot and Wolffson (1952), who showed that the average daily output of urinary 17-ketosteroids from the adrenal cortex in 37 West Africans was distinctly less than in Europeans.

Conclusion

A difference in endocrine balance between Africans and Europeans has been postulated in the past because of certain observed differences in morphological, physiological, and pathological patterns. For example, in East Africans blurring of skeletal sexual differences is the rule, and idiopathic eosinophilia is common, but coronary atheroma and psoriasis are rare.

I have shown that there is a clear-cut reduction in the adrenal cortical masses in East Africans compared with Europeans, which does not apply to the adrenal medulla. This may have an important bearing on the constitution and diseases of East Africans.

I wish to thank Prof. Alexander Galloway for facilities in the department of anatomy, Professor Davies for access to post-mortem weight records, and Dr. R. F. A. Dean for valuable discussions on the measuring techniques used.

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FŒTAL DEATH IN UTERO WITH HYPOFIBRINOGENÆMIA
MANAGED CONSERVATIVELY

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IN obstetric hæmorrhage with defective coagulation of the blood the most consistent finding is a low fibrinogen level, occasionally associated with deficiencies of other coagulation factors. Failure of coagulation most commonly occurs with (1) premature separation of the placenta, (2) eclampsia, (3) retention of dead fœtus or placental fragments, or (4) embolism of amniotic fluid.

Weiner et al. (1950) seem to have been the first to recognise the condition in association with retention of a dead fœtus. They thought that rhesus incompatibility might be responsible for the coagulation defect, the fœtal deaths in their obstetrical cases having been attributed to this. Later work has not confirmed this suggestion.

Barry et al. (1955), O'Driscoll and Lavelle (1955), Klein et al. (1956), and Howie (1956) have reported single cases associated with retention of the dead fœtus. In most of these the diagnosis was made only after the hæmorrhage.

Pritchard and Ratnoff (1955) point out that the development of hypofibrinogenæmia in patients with retained products of conception is probably slow, taking at least 4–5 weeks after the death of the fœtus. This contrasts with the sudden development which seems to characterise hypofibrinogenæmia from other causes. These workers record that of 31 women in whom the fœtus died in utero only 8 developed severe fibrinogen deficiency, 3 of them presenting with either spontaneous hæmorrhage or bruising. However, 7 on whom serial observations were done showed a progressive fall in the fibrinogen level—though this did not reach the critical level for spontaneous hæmorrhage (somewhat arbitrarily suggested by various workers to be 100 mg. per 100 ml.).

The management of the condition has varied. Pritchard and Ratnoff (1955) recommend induction of labour as soon as the fibrinogen level falls, and hysterotomy if the attempt at induction fails. Other obstetricians deprecate any form of delay and recommend early hysterotomy (or even hysterectomy). We report here a case in which a more conservative method was adopted.

Case-report

Mrs. H, aged 35, first attended the antenatal clinic on Aug. 11, 1955, at the 24th week of her tenth pregnancy, having been referred by her own doctor because of a history of rhesus incompatibility. She had given birth to five children: the first and second had been unaffected; the third survived after an exchange blood-transfusion; and the fourth and fifth had died in the neonatal period in spite of exchange transfusions. She had also had four miscarriages, the last being just before the 28th week in her ninth pregnancy, in 1954.

The fœtal heart was inaudible, and the patient said that she had not felt movements. Yet the uterus was enlarged to a size consistent with the period of amenorrhœa; and X-ray examination revealed a fœtus which corresponded to a maturity of 23–24 weeks, and there was no clear evidence of fœtal death. She was asked to attend at fortnightly intervals for observation.

On Oct. 3 it was definitely recognised that the uterus was not increasing in size. The fœtal heart remained inaudible, and she had felt no movements. During the previous three days she had noticed sudden spontaneous bruising below her right eye and on her lower limbs, especially the front of the left thigh. She was immediately admitted for investigation.

On admission radiological examination confirmed intra-uterine death of the fœtus.

Hæmatological Investigations

The blood was group-A and rhesus-negative, with strong incomplete antibodies. Hæmoglobin 77% (11·4 g. per 100 ml.), packed cell volume 36%, mean corpuscular Hb concentration 32%, platelets 240,000 per c.mm. A film showed some anisocytosis of the red cells and abundant platelets. Bleeding-time (Duke) 4 min. 30 sec.; no clot after 1 hour at 37°C. Plasma-fibrinogen level 76 mg. per 100 ml.; plasma clotting-time $2^1/_2$ min. (normal $1^1/_2$–$3^1/_2$ min.); one-stage prothrombin-time 22 sec. (normal 12 sec.); after the addition of fibrinogen the time was 13 sec., indicating that there was no deficiency of prothrombin or of factors v and vii (Dr. H. Lempert). Results of tests for fibrinolysis were inconclusive. No deficiencies in other coagulation factors were found (Dr. R. L. Turner).

A diagnosis was made of hypofibrinogenæmia in association with fœtal death in utero, the dead fœtus having been retained for at least 8 weeks.

Progress

In the week following admission there was further spontaneous bruising, chiefly over the arms and anterior abdominal wall. Venepuncture was complicated by subcuticular ecchymoses. Daily estimations of fibrinogen revealed no significant change.

In the second week the patient's general condition was satisfactory. Spontaneous hæmorrhages were slight and were restricted to the areas in contact with a bedpan. Fibrinogen was estimated on four occasions. The hope that it would increase spontaneously was not realised. Nevertheless it was decided to await if possible the spontaneous onset of labour. Compatible blood and fibrinogen were held in readiness to treat any emergency.

Subsequently the spontaneous hæmorrhages virtually ceased, the only ones recorded being 4 weeks and 6 weeks after admission; they were very small and occurred over the right buttock and right femoral trochanter. The patient's general condition remained satisfactory. There was no fall in hæmoglobin. The platelet count remained within normal levels. The fibrinogen was estimated twice or thrice weekly, and its level did not change appreciably.

On Oct. 28 (25 days after admission) a test dose of fibrinogen 2 g. was given intravenously to see whether it would influence the estimated systemic level, and (if so) for how long. Fig. 1

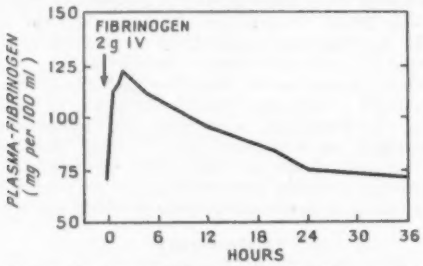

Fig. 1—Changes in plasma-fibrinogen levels after intravenous administration of fibrinogen 2 g.

shows that, though the increase of fibrinogen was rapid (from 70 mg. to 123 mg. per 100 ml. in 105 minutes) and of the order expected for this quantity of fibrinogen, the higher level was not maintained: indeed the fibrinogen fell below 100 mg. in 12 hours and returned to its previous level in 24 hours.

No further action was taken until the expected date of delivery (Nov. 30) had passed without spontaneous onset of labour. On Dec. 4 labour was successfully induced with quinine, castor oil, and an oxytocin drip, the dead fœtus being delivered within an intact sac about 24 hours later. There was no retroplacental clot. About 50 ml. of fresh blood was lost during the first stage of labour and a further 300 ml. immediately before delivery. Intravenous and intramuscular ergometrine was given immediately after delivery, but the uterus tended to relax with further loss per vaginam. The oxytocin drip was therefore continued for 4 more hours to a total quantity of 15 units of oxytocin, of which 11 units preceded delivery. Oozing per vaginam ceased about 7 hours after delivery. The pulse-rate remained about 96 per min., but the blood-pressure fell to 80/60 mm. Hg 2 hours after

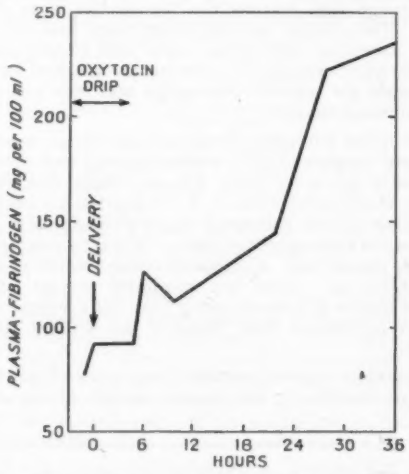

Fig. 2—Plasma-fibrinogen levels after delivery of fœtus.

delivery. The patient's condition was not alarming, however, and began to improve before the oozing had ceased completely. Every effort was made to measure the exact post-partum loss. The quantity collected was 500 ml., making with the estimated antepartum loss a total of 850 ml.

Fibrinogen was estimated on six occasions in the first 12 hours and frequently thereafter. Fig. 2 shows the gradual return to normal over 36 hours. The cessation of the vaginal loss corresponded roughly with the attainment, 6 hours after delivery, of a level of 126 mg. per 100 ml.

2 days after delivery the hæmoglobin was 47%. But 2 days later it had fallen to 39% without further external bleeding and without evidence of intraperitoneal hæmorrhage. The fibrinogen level by this time was 364 mg. per 100 ml. Because of the anæmia the patient was transfused, after which her convalescence was rapid and uneventful, and she was discharged on Dec. 23 with a hæmoglobin of 75%. On attendance at the postnatal clinic on Feb. 13 the hæmoglobin was 86%.

Discussion

In retrospect it was considered that the fœtus perished at the 24th week and had thus been dead for 8 weeks when the clinical signs pointing to hypofibrinogenæmia were recognised. Thereafter the fibrinogen level was persistently low for the next 8–9 weeks but after delivery it rose spontaneously to normal without administration of any fibrinogen and without blood-transfusion.

The reason for adopting a conservative policy requires some examination, since the risk of further spontaneous hæmorrhage had to be accepted. It was at first thought possible that the fibrinogen level might improve spontaneously. As hope of this was abandoned, it was then thought better to allow the uterus to empty itself spontaneously and at maximum muscular efficiency rather than to attempt the artificial induction of labour at a time when the response of the uterine muscle might be sluggish. The alternative of emptying the uterus by hysterotomy or of carrying out hysterectomy was considered too major.

The fate of the test dose of fibrinogen is of interest. The return to the previous level within 24 hours is striking. It may indicate the persistence, 11–12 weeks after the death of the fœtus, of an active process capable of removing at least 2 g. of fibrinogen from the circulation within 24 hours. Whether a larger dose of fibrinogen would have maintained for a longer period a level sufficiently high to justify induction of labour remains uncertain. This must not be interpreted as criticism of the administration of fibrinogen as a prophylactic measure after labour has become established.

As regards the management of labour, the risk of disastrous bleeding was believed to be small. Judging

by the figures of Pritchard and Ratnoff (1955), fibrinogen deficiency associated with intra-uterine death is not uncommon, whereas intractable postpartum hæmorrhage is rather rare in the untreated case of intra-uterine death. It was therefore felt justifiable to withhold fibrinogen at the time of delivery, especially as many workers have reported control of bleeding after a dose of fibrinogen as low as 0·2 g. (Barnett and Cussen 1954, FitzGerald and Jackson 1956, Kimbell and Ghosh 1956). This suggests that some other factor than exogenous fibrinogen might suffice for hæmostasis. In the event bleeding was considerable. It is debatable whether the postpartum loss would have been kept down to 500 ml. if the oxytocin drip had been discontinued. Our impression is that the drip was definitely valuable in assisting the uterine muscle to control the blood-loss until the patient's fibrinogen reached the level at which coagulation took place. On the other hand, Howie (1956) has pointed out the theoretical objection that the use of oxytocin might express into the maternal circulation increased quantities of a noxa which previously had been rather slowly absorbed. We were (rightly or wrongly) surprised at the 6 hours which elapsed after delivery before the fibrinogen level began its rapid ascent, and are inclined to conjecture that oxytocics may have played a part in delaying recovery. But it must be remembered that this patient was exposed for an exceptionally long period to the still unexplained mechanism of fibrinogen depletion, and it may be that any unusual delay in return to normal could be more correctly attributed to the prolongation of that period of exposure.

Summary

A case of hypofibrinogenæmia in association with fœtal death in utero is reported.

Spontaneous bruising was noticed about 8 weeks after the fœtus had perished.

The mother was treated conservatively for 9 weeks more before labour was induced medically.

Delivery was followed by a spontaneous return to normal levels of the blood-fibrinogen.

The reasons for adopting a conservative policy are discussed.

We thank Prof. W. I. C. Morris for permission to publish this case and for advice and criticism in the preparation of this paper; also Dr. M. C. G. Israëls for his advice; and to Dr. H. Lempert for the fibrinogen estimations.

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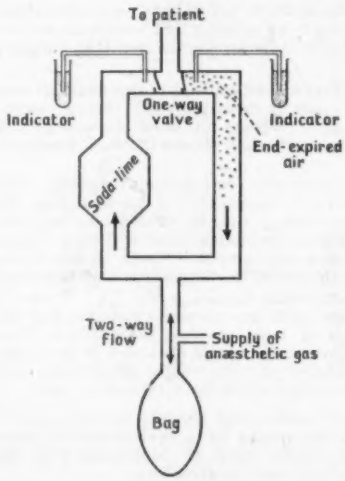
New Inventions

SIMPLE AUTOMATIC SAMPLER OF END-EXPIRED AIR FOR PRESSURE BREATHING

DURING anæsthesia assisted by pressure ventilation with gas containing a high concentration of oxygen, anoxæmia is easily prevented by maintaining ventilation at a rate and depth sufficient to keep the patient pink. Recognition of carbon-dioxide accumulation and acidæmia, or of carbon-dioxide deficit and alkalæmia, is more difficult. Ventilation volumes sufficient to provide an adequate uptake of oxygen may yet be insufficient to prevent the retention of carbon dioxide in the lungs and blood. On the other hand, over-ventilation may blow off carbon dioxide faster than it is formed in the body. This will lead to carbon-dioxide partial pressures in lungs and blood lower than usual for the patient.

A simple automatic indicator of alveolar carbon-dioxide concentration would help to prevent these extremes. It would also be of use in the management of patients with respiratory paralysis.



A suitable sampler and indicator may easily be made from equipment common to most anæsthetic departments or otherwise easily obtained. The apparatus automatically extracts small amounts of end-expired air from the circuit and bubbles them through a coloured indicator solution. The composition of this end-expired air closely resembles that of "alveolar air."

The patient breathes through a one-way valve into the anæsthetic circuit; a loop with a soda-lime canister on the inflow side. During the pause following expiration, end-expired air rests in the outflow arm of the loop. Inspiration takes place when the anæsthetist (or the ventilation machine) increases the pressure in the loop by squeezing the bag. This drives the gases through the carbon-dioxide absorber and along the inflow arm into the patient's lungs. The gas in the outflow arm is trapped by the outflow valve, and a small amount is forced through the sampling needle to bubble through the indicator solution. The rise of pressure in the outflow loop during expiration is too small to force gases into the indicator.

The outflow arm should be long enough to accommodate about $1^1/_2$ times the tidal volume. The theoretical objection to the use of valves near the patient's mouth is that moisture may make them stick. This can be prevented quite simply by covering the valve seating with sticking-plaster. Spring-loaded plastic valves are even better. The end-expired air may be tapped off by sticking a no. 14 or a no. 12 needle into the tubing near the outflow valve. The indicator solutions and a simple holder and colour comparator for them may be bought quite cheaply.

It is of more than incidental interest that this loop very efficiently delivers carbon-dioxide-free gas to the patient. This can be checked by a sampler in the inflow arm.

The colour of the indicator solution reflects the concentration of carbon-dioxide in the gas bubbling through it. There is a delay of about half a minute. The reaction is reversible. The response scale of the solutions varies with their composition. We use solutions sensitive to 0·3–5·0% carbon dioxide on the inflow arm and 0·6–10·0% carbon dioxide on the outflow arm. In practice great accuracy is not required. By colour matching, changes of 0·5–1·0% in the concentration of carbon dioxide are easily recognised.

This apparatus has been giving satisfactory service at the London Chest Hospital for some months.

We wish to thank Dr. R. Beaver and Dr. J. Smart for permission to publish and Dr. L. O. Mountford for his help and encouragement. Dr. A. Bracken, of the British Oxygen Co., kindly supplied the indicators.

L. H. CAPEL
M.B. Lond., M.R.C.P.
D. C. HODGSON
M.B. Lond., D.A.
London Chest Hospital

Reviews of Books

Principles of Chest X-Ray Diagnosis

GEORGE SIMON, M.D., F.F.R., assistant director, X-ray Department, Brompton Hospital, London. London: Butterworth. 1956. Pp. 174. 50*s*.

THIS is an extremely interesting book, well written, well illustrated, and containing many original observations.

About two-thirds of it is devoted to the X-ray changes in diseases of the lungs, including sections on bronchography and tomography, with two small and relatively unimportant chapters on the heart and mediastinum respectively.

The strength of the book rests on the sections on the lungs, and at least part of the interest lies in the method of presentation of the material. Instead of following the customary plan of describing the radiological changes seen in different diseases, Dr. Simon has classified the shadows seen in lung films into different types. Thus the chapters are headed "homogeneous shadows," "linear shadows," and so on; and under each of these headings the different causes of the appearances and their differentiation are discussed. The descriptions are accurate, the differential diagnoses are usually full, and the discussion is always of a high standard.

This approach is, of course, eminently practical and will make an immediate appeal to those concerned in the radiological diagnosis of diseases of the lungs. The author assumes that his readers have a considerable knowledge and experience of radiology, and it is probably true to say that the more experienced the reader the more he is likely to get out of the book. For the same reason and because no attempt is made to cover all diseases of the lung systematically, it may not be so suitable for students; but to the practising radiologist and to the chest physician it will be of considerable value.

The Life of Hugh Owen Thomas

DAVID LE VAY, M.S., F.R.C.S., orthopædic surgeon, S.E. Metropolitan Region. Edinburgh: E. & S. Livingstone. 1956. Pp. 135. 25*s*.

MOST medical students and many doctors, asked what they knew of Hugh Owen Thomas, would say that he was "a Welsh bone-setter." This in spite of the fact that he was probably of Spanish descent, and that, as a qualified surgeon, he spent most of his professional life in vigorous polemics against "bone-setters." But popular biographers have not served him well, and Mr. Le Vay's work is very welcome.

Thomas practised in Liverpool from 1858 until his death in 1891. At this time that city, with its constantly changing population of hard-bitten sailors and uncouth immigrants, had an atmosphere likened to that of a frontier town. The skirmishes between Thomas and his contemporaries strengthen the comparison. But Thomas stood also at a frontier in time. He can be seen—and how fittingly—as the ultimate figure in an era when diagnosis was instinctive and treatment empirical. He lived to see the dawn of bacteriology, to see his "strumous joints" positively identified as tuberculous. Only five years after his death, and in his own consulting-rooms, his nephew took the first radiograph of a patient ever prepared in this country. Thereafter a surgeon could not practice by the use of his unaided senses alone.

But this does not imply that Thomas's teachings cannot be profitably studied by a later generation. We hope that the suggestion, mentioned in the preface to this book, of publishing his collected works in a modern edition will come to fruition. Because Thomas always considered himself essentially a general practitioner, such an edition would have an appeal outside the surgical community.

Many of Thomas's teachings Mr. Le Vay has himself taken to heart, and it is apparent that this book has been a labour of love. It contains references to much previously unpublished material, and evidence of painstaking scholarship and personal research. It is written in an easy style, and it has the fascination that keeps the reader engaged long after bedtime. Some may regret that after the last page, they still know little of Owen Thomas, the man. Of that saturnine and restless individual, with his passion for bananas, and his nightly inability to sleep until his wife had played the *Dead March in Saul*. The fault is not Mr. Le Vay's. A later generation may never understand Hugh Owen Thomas. Perhaps he did not understand himself.

Noradrenaline

Chemistry, Physiology, Pharmacology and Clinical Aspects. U. S. VON EULER, M.D., F.A.C.P. (HON.), professor of physiology, Faculty of Medicine, Karolinska Institutet, Stockholm. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1956. Pp. 382. 87*s*. 6*d*.

NORADRENALINE has been known as a chemical entity since 1904, but not until 1946 was it realised that this substance occurs naturally in animal tissues. Two workers separately and almost at the same time made this observation. One of them was P. Holtz and the other U. S. von Euler, who has now written this monograph.

After a brief historical résumé the book passes to a consideration of the chemical properties of noradrenaline, and thence to its formation and inactivation in vitro and in vivo. Reference is made to the new techniques of chromatography, ion-exchange resins, and counter-current systems which have been fully employed for separating and estimating noradrenaline from mixtures, and have given valuable information regarding the tissues in which noradrenaline is found and its concentration both in them and in body-fluids. But, as von Euler points out, we are still uncertain just how the body makes noradrenaline and why in some circumstances this important substance can be made rapidly and in others only slowly.

von Euler's own work has done much to prove that noradrenaline is the major sympathetic transmitter, though other related compounds may be released at a few special sites. It must be present in the blood-stream, but its concentration there is low and its estimation therefore difficult and inaccurate. Fortunately its presence in urine (as was shown by the author) is easier to estimate, and is related to the amount produced in the body. The last chapter deals with therapy and the undoubtedly beneficial effects of noradrenaline in certain hypotensive states.

This interesting book not only shows how much work has been done on noradrenaline, but offers many problems to those with the time and inclination for research.

Living Bone in Health and Disease

IRVIN STEIN, M.D., F.A.C.S., assistant professor of orthopædic surgery, University of Pennsylvania; RAYMOND O. STEIN, M.D., F.I.C.S., chief of orthopædic surgery, Doctors Hospital and Sidney Hillman Medical Center, Philadelphia; MARTIN L. BELLER, M.D., assistant chief of orthopædic surgery, Philadelphia General Hospital. Philadelphia: J. B. Lippincott. London: Pitman Medical Publishing. 1955. Pp. 510. £5 10*s*.

IN their preface the authors hope that "a presentation of the picture of living bone will suggest many clinical as well as research possibilities to the thoughtful surgeon and physician."

The first part of the book is an account of the structure and physiology of bone; part II deals with the clinical, radiological, and pathological aspects of bone diseases; and part III is a "diagnostic clarification of bone disease," presented in a series of tables.

The authors are primarily orthopædic surgeons, and considering the increasing complexity of modern work on bone physiology and pathology, they have taken on a big task. The competent accounts of the clinical aspects of bone disease are illustrated by many radiographs. There is also much useful biochemical information, the diagnostic significance of which is summarised in tables.

The sections dealing with the normal structure and the pathological histology of bone are less satisfactory. The chapter on the gross and microscopic structure of bone and cartilage contains a number of controversial statements; and the selection of illustrations might have been more apt.

In its clinical and biochemical aspects this is a sound book; and the authors might have been better advised to leave it at that rather than to tackle as well the intricacies of pathology and morphology.

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THE LANCET
LONDON: SATURDAY, SEPT. 22, 1956

Metabolism of Iodotyrosines

RECENT research has embroidered, but not radically changed, HARINGTON's now classical concept [1] of the biosynthesis of thyroid hormone. The first step is thought to be the iodination of tyrosine radicals, within the thyroglobulin molecule, to form iodotyrosines. Some of these then couple to give thyroxine. But only a proportion can do so, depending on their spatial position within the thyroglobulin molecule. When the thyroglobulin molecule is later hydrolysed by the protease known to be present in the gland, mono- and di-iodotyrosines must be released, as well as the active hormonal products, thyroxine and triiodothyronine. Yet only the two last compounds appear in the blood. Mono- and di-iodotyrosine apparently disappear, since only traces of the free compounds can be found within the gland. The mystery of the vanishing iodotyrosines was solved by ROCHE and his colleagues,[2] who discovered an enzyme in the thyroid which has the property of liberating iodine from mono- and di-iodotyrosine. This deiodinase acts only on iodotyrosines; it has no action on thyroxine or any of the other iodinated thyronines. Since it is activated by thyroid-stimulating hormone and depressed by thyroxine,[3] it is likely to have an important part to play in the economy of the thyroid. Its presumed function is the conservation of iodine, which would otherwise be lost to the thyroid if it was allowed to escape in the form of iodotyrosines. Even if these substances were deiodinated elsewhere in the body, only about half the iodine contained in them would find its way back to the thyroid as iodide, the rest being excreted in the urine. Since a large proportion of the iodine in thyroglobulin is contained in iodotyrosine radicals, the amount which could be lost, in the absence of the deiodinating enzyme, would be quite considerable. Even in areas where there is no endemic goitre the intake of iodine in the diet is not much more than barely adequate. It is therefore to be expected that the absence of the deiodinating enzyme would result in the signs of iodine deficiency, shown first by the development of a hyperplastic goitre and later by hypothyroidism.

This expectation has now been verified by STANBURY and his colleagues,[4] working in Professor QUERIDO's laboratory at Leyden. They have described 3 cases of goitre with hypothyroidism which appear to be adequately explained by presuming a congenital absence of the deiodinase. After giving these patients iodide labelled with ^{131}I, mono- and di-iodotyrosine were identified in the blood and urine. This showed that the deiodinating enzyme was either absent or not doing its job properly. This would not necessarily be a serious matter for the patients if they could split off the iodine elsewhere in the body, since about half of it would then find its way back to the thyroid. But they were not able to do so, for when labelled di-iodotyrosine was given intravenously it appeared almost entirely unchanged in the urine. This is in sharp contrast to what happens in normal people who can split off all the iodine from administered di-iodotyrosine. Similarly, when mono-iodotyrosine was given to the 3 goitrous patients, the bulk of it appeared in the urine either unchanged or in the form of unidentified iodine-containing substances. The clinical features in these 3 cases can probably be explained by the assumption that the patients had no deiodinating enzyme either in the thyroid or elsewhere in the body. The loss of iodine resulting from continual excretion of iodotyrosines in the urine might well be sufficient to prevent the formation of thyroid hormone in adequate amounts, even by enlarged and hyperplastic glands.

Of the 3 patients, 2 were brothers. The 3rd was not related to the other 2, but 4 of her own relatives had goitres. These were investigated, together with a 5th unaffected member of the family. These 5 were able to deiodinate intravenous di-iodotyrosine, but less efficiently than normal subjects. It is a fair guess that the defect was enough to stimulate goitre formation and that the enlarged thyroid was then able to make sufficient hormone, in spite of its handicap, to avoid clinical hypothyroidism. The cases studied by STANBURY et al. were too few to permit deductions about genetics. A biochemical defect of this sort is, however, likely to be genetically determined, and it is tempting to consider the possibility that the 3 patients with the full defect represent homozygotes, while the relatives with goitre, but no hypothyroidism, may be heterozygotes. Much more work would be needed to test this idea, but it is interesting as a possible explanation of the far from negligible number of goitres which appear in areas where the supply of iodine is apparently adequate. Although the supposed homozygotes, with complete lack of deiodinase, are obviously rare, it is quite possible for the beterozygotes to be relatively common. These speculations are running a long way ahead of the evidence, but they suggest that it might be worth applying the techniques developed by STANBURY et al. to the investigation of other cases of non-endemic goitre.

1. Harington, C. R. *Proc. roy. Soc.* B. 1944, **132**, 223.
2. Roche, J., Michel, R., Michel, O., Lissitzky, S. *Biochim. biophys. Acta*, 1952, **9**, 161.
3. Michel, R. *Amer. J. Med.* 1956, **20**, 670.
4. Stanbury, J. B., Meijer, J. W. A., Kassenaar, A. A. H. *J. clin. Endocrin.* 1956, **16**, 848.

Undescended Testis

THE lack of accurate information on postnatal descent of the testis has lately been emphasised by SCORER.[1 2] He followed up 1700 male infants first seen at a maternity unit and compared his figures for incomplete descent at the end of the first year of life with those for the adult population, as calculated by SOUTHAM and COOPER.[3] Their estimate for the general population was near to SCORER's observed prevalence in infants, and from this he concludes that "it seems likely that complete descent of the testicles does not occur after the age of three months."

If this is true, it is an important piece of information and may lead to a change of views on the best time for treating the undescended testis. But to accept

1. Scorer, C. G. *Arch. Dis. Childh.* 1956, **31**, 198.
2. Scorer, C. G. *Brit. J. Urol.* 1955, **27**, 374.
3. Southam, A. H., Cooper, E. R. A. *Lancet*, 1927, **i**, 805.

it we must refute the experience of many clinicians who have seen descent at a later age, and we must also accept SOUTHAM and COOPER's figures, compiled in 1927, as the last word on the subject. They arrived at their estimate of incomplete descent of the testis in adults from recruiting-board figures in Scotland, the Austro-Hungarian Empire, and the United States, as well as from hospital-admission figures. They made no observations themselves, and even their estimate—a mean of widely divergent figures—refers only to unilateral cryptorchidism. SCORER's arguments raise the question of how surely the testis can be located in the newborn. SCORER says that there has never been any difficulty in deciding the position of the testis, providing it is outside the external abdominal ring; and he points out that the cremasteric reflex is not strong in the newborn. It could be, however, that his large experience enables him to do with ease what others find some difficulty in doing. The greatest problem in any discussion on undescended testicles is to exclude the retractile testis,[4] for which no treatment is required except categorical reassurance, and which in older boys has certainly fooled many doctors and even experienced surgeons many times. Over half the patients sent to outpatients for treatment are in this category. If the retractile testis is "treated" the "results" are bound to be good, and it is vital to exclude this type from the discussion.

Hormones and surgery are both used in the treatment of undescended testicles, but there is little agreement on the place or timing of either measure. Perhaps the only widely held view is that treatment must be started before puberty if it is to be effective. Even then some will say that any improvement that follows might have taken place later anyway. If we could say that no testicular descent takes place after a certain age, that would be a firmer basis for treatment; and for this reason inquiries such as SCORER's are especially welcome. Many surgeons use hormones, particularly, as MACNAB [5] points out, as a diagnostic test. Those who do so feel that they encourage descent of the normal testis, while they can have no action on the mechanically tethered gland. But there may be more support for LOUW's view [6] that hormones should probably be reserved for patients of the Fröhlich type with bilateral undescended testicles and genital hypoplasia.

It is fortunate that unilateral cryptorchidism is far the commoner problem. Orchidopexy for unilateral incomplete descent or unilateral ectopic testis is undertaken as much for cosmetic or psychological reasons as to put the tethered organ out of harm's way. HANSEN [7] has shown by his careful studies that, in unilateral maldescent, orchidopexy has no effect on the quality or quantity of the sperm-counts. Most surgeons like to operate when these patients are 9 or 10 years old, but there is a move, supported by the histological findings, towards earlier surgery. HINMAN [8] summarises recent histological investigations by saying that up to the age of 6 years microscopic changes in the undescended testis are few, but from then on the differences between normal and undescended testicles are progressive. On the other hand, the larger the patient the less likelihood there is of damaging the blood-supply through the testicular artery, which is the usual limiting factor in the operation. As for bilateral undescended testicles, the best published results, judged from the important viewpoint of fertility, seem to be those of GROSS and JEWETT.[9] Of 38 men who had had the bilateral operation between the ages of 9 and 11 years, 79% proved fertile. Until these results are bettered, this will probably remain the age of choice.

There is no doubt that some testes will never function, regardless of hormonal or operative treatment. The shape, size, and consistence of the organ are more important than its position. If it is soft and flabby at operation or hard afterwards, it is unlikely to be functioning normally. But further critical inquiries into the natural history of the condition are needed, before we can be sure what effect treatment is really having.

The Edinburgh Venture

IT has been said that, as a nation, we are better at planning than putting into action the plans we make; and that we tend to underestimate our own academic achievements. It is perhaps fitting, therefore, that an account of the Edinburgh University general-practice teaching unit, written by the unit's director, Dr. RICHARD SCOTT, should appear in the American *Journal of Medical Education* this month. The teaching of general practice to students in Edinburgh University is, in fact, as old as the United States itself, for the Royal Dispensary was founded in 1776, the year of the Declaration of Independence, and until 1948 this dispensary provided medical care for the "sick poor" of the city. Generations of medical students have received their introduction to general practice in the Edinburgh dispensaries, where they have been taught by many of the most distinguished teachers of their day. When the National Health Service was planned, there was no place for the particular blend of care and teaching which the dispensaries had perfected, for complete medical cover was provided by the general-practitioner side of the N.H.S. The obsolescence of the dispensaries was at once an opportunity and a challenge, and we know with what inspiration that challenge was met. Two dispensaries, each with its group of people who looked to it for medical care, were taken over as general medical practices, well equipped and staffed by the university. The patients could get the same range of care as they could by registering with a general practitioner in the ordinary way. Thus, the tradition of service to man and to medicine continued unbroken.

The teaching responsibilities of the general-practice teaching unit have increased its need for staff and accommodation, and generous help from the Rockefeller Foundation made expansion possible. Each practice is now staffed by two doctors, a nurse, a medicosocial worker, and a secretary; and a dispenser attends at one of the centres. The population served by each team is no more than 2500, so that the practices are strongly staffed; but that enables 60 students

4. Browne, D. *Brit. med. J.* 1938, ii, 168.
5. Macnab, G. H. *J. R. Coll. Surg. Edinb.* 1955, **1**, 126.
6. Louw, J. H. *S. Afr. med. J.* 1954, ii, 807.
7. Hansen, T. S. *Proc. R. Soc. Med.* 1949, **42**, 645.
8. Hinman, F. *Fertil. Steril.* 1955, **20**, 214.
9. Gross, R. E., Jewett, T. L. *J. Amer. med. Ass.* 1956, **160**, 634.

in each academic year to be given an insight into the problems of general practice in a way which must surely be unique. Certainly the students have no doubts about the merits of the three-month course, and applications exceed vacancies. Those selected are introduced to patients at first in consulting sessions and later on home visits with one of the doctors in the team. Each student is given progressively increasing responsibility for the care of one or two patients, under the supervision of the doctor, and at case-conferences and tutorials he is given opportunity to display his grasp of the things that cause or aggravate the illness of the patient in his charge. This is a new approach to a clinical situation for many students, who have not previously considered the relative importance of social as well as clinical factors in an illness or family situation. Some of the methods used —case-work, seminars, and group conferences— are modified from American patterns, and achieve their purpose well as a Scottish interpretation.

Though the population served by the two practices does not accurately reflect the social distribution of the population as a whole, the two communities are nevertheless being used for observational research, particularly in that province somewhere between those of the strictly medical and the strictly social workers—a field which may prove very fruitful in helping to understand the environmental causes of disease. In the unit the student can see field research in general practice, the recording of morbidity in the family context, and the interpretation of findings in preventive terms. The old dispensary, once limiting its service to advice and medicines, is now a growing-point of public health as well.

In other university cities where there used to be dispensaries, opportunities for medical teaching may have been lost, for the potential practices surrounding the dispensaries have by now dispersed. There is still a chance, however, to develop the further teaching of general practice by absorbing active practices into the university or medical school, and increasing their staff, as Edinburgh has done, to allow them to carry a full teaching load. A teaching practice need not necessarily be based upon a dispensary; and the social background to general practice would be more accurately presented by a practice in which all social groups were represented. The next evolutionary stage may be the university department of general practice, which would coördinate the teaching and research work in a number of practices, demonstrating not only urban and suburban conditions but those of country practice too.

Annotations

CARING FOR EPILEPTICS

As Hippocrates said, epilepsy is a disease unlike any other disease, and epileptics are equally, by ancient tradition, people set apart. This unhappy apartheid was curiously perpetuated in the framing of the National Health Service; and a subcommittee of the Central Health Services Council, under the chairmanship of Lord Cohen of Birkenhead,[1] has lately pointed out many defects in the care given to epileptics and has suggested ways in which the defects might be remedied.

At present the care of epileptics is haphazard: some get no treatment and others get too much. Some are treated by their family doctors only; others wander between the general physician, the pædiatrician, the neurologist, the neurosurgeon, and the psychiatrist. The report of the Cohen committee makes plain that this is a matter in which the coördination of many specialties is essential and in which, in fact, a coördinated service is at present lacking. The committee recommend that special clinics and centres be set up at which epileptics may have the necessary investigations and from which their medical care and social rehabilitation may be supervised. Apart from closing a disturbing gap in the provisions of the National Health Service, such centres would be an economic asset, for many adult epileptics have drifted down the social ladder for lack of adequate support and wasted their abilities in dead-end jobs; and many affected children have been excluded unnecessarily from ordinary schools and given residential care that they did not really need. The British Epilepsy Association has already done magnificent work in preventing such tragedies and in breaking the taboos that bar epileptics from normal life. There is no doubt that the association will be glad of the opportunity to extend its work in partnership with the new centres.

The committee criticise the arrangement whereby epileptic colonies were excluded from those institutions which were taken over by the National Health Service under the 1946 Act: rightly so, for the whole idea of a colony of permanent inmates is now seen to be wrong. The colonies should be, and no doubt wish to be, centres for active treatment and rehabilitation: as such, they should be integrated with other hospital services. Whether this will now be possible is uncertain. Fresh legislation would be needed and this might raise political difficulties. Yet it is hard to see why there should be a permanent bar to the inclusion of the colonies in the National Health Service; but if there is the committee suggest that friendly arrangements between each colony and its local regional hospital board might meet the case.

The committee's terms of reference did not allow them to discuss the linked questions of prophylaxis and of research: yet these are matters which must concern the new service. Most of the recent research into epilepsy has dealt with the minutiæ of electrophysiology and neurosurgery; and background research into the natural history of the convulsive disorders has been much neglected in this country. For example, we have no firm definition of the word "epilepsy": different people mean different things. There is no agreed classification of the many varieties of epileptic experience, nor are their prevalences known. We do not know exactly what the problem is we are trying to tackle or how big it is. Questions of ætiology, and in particular the influence of hereditary factors, are raised by patients and their relatives in every clinic; but no reliable answers can be given. And prognosis is equally vague.

The plan proposed by Lord Cohen's committee will offer very rewarding tasks to those who put it into action, and it will give new encouragement to epileptics.

1. Ministry of Health, Central Health Services Council, Report of the Subcommittee on the Medical Care of Epileptics. H.M. Stationery Office, 1956. 1s. 6d.

TINEA CAPITIS

DURING the early years of this century tinea capitis was a considerable problem to local health authorities. The infection was commonly due to *Microsporon audouini*, which affects only children and disappears spontaneously at the age of puberty. Its diagnosis is relatively easy since one or more scaly patches appear on the scalp, and hairs are regularly broken off $^1/_8$ in. above the surface. The infected hair stumps fluoresce under Wood's light and the mycelial threads are easily

visible under the microscope. The standard treatment has been X-ray epilation of the whole of the scalp hair, accompanied by the daily application of a fungicide, such as Whitfield's ointment, until all infected hairs are shed. The child was excluded from school and a close-fitting washable cotton cap was worn until freedom from infection was established. This type of ringworm has become increasingly uncommon during the past fifteen years and apart from a small recrudescence during 1945–47 it is now rarely seen in the United Kingdom.

A new form of tinea capitis due to *Trichophyton sulphureum* has lately emerged, and although it is still comparatively uncommon it is increasing in prevalence. In 1950 Walker,[1] working in a reference laboratory, isolated *T. sulphureum* 39 times from 2473 cultures; and in 1952 Partridge [2] isolated this fungus from 15 of 179 cases of tinea capitis. It is difficult to draw conclusions from figures given by some other observers because they include several species under the generic name *Trichophyton tonsurans*. During a period of seven years Beare [3] in Belfast collected 82 cases of scalp ringworm in children (45 boys and 37 girls) caused by *T. sulphureum* which had been confirmed by culture.

T. sulphureum is a parasite confined to man. Unlike *M. audouini*, the reaction which it produces on the scalp varies from nothing in about 50% of cases to severe inflammation resulting in kerion in over 10%. The infections with no reaction are very hard to diagnose because the patches may be tiny with only an occasional infected hair which may be broken off at any level. Clinically this state may be indistinguishable from patchy seborrhœic dermatitis. Scaling is usually present within the infected area, which may show various degrees of inflammation. Unfortunately *T. sulphureum* does not fluoresce under Wood's light, although affected hairs will often look dull compared with normal hair. It is not surprising that Beare [3] seldom succeeded in tracing contact cases since many mild ones must pass unnoticed by both parent and doctor. This is in striking contrast to microsporon infections.[4]

Delayed reactions may sometimes follow after two or three months. The change in the reaction from non-inflammatory to severe inflammatory is usually the result of hypersensitivity produced by the fungus on the skin, rather than the result of local fungicidal treatment. Sometimes delayed kerion may follow trauma such as a blow, or radiotherapy. Parents may well attribute the temporary deterioration in the child's condition to radiotherapy, although the kerion will hasten what may otherwise be a protracted course of many months.

Beare [3] does not consider X-ray epilation, with its theoretical risks, justifiable if the ringworm is causing no symptoms and is difficult for the parents to detect, even though he appreciates the dangers of the carrier state. Thorne and Grange,[5] who followed for five years 365 cases of microsporon infection treated by X-ray epilation, did not find any evidence of danger to the scalp; but they emphasised that children under the age of 5 should not be irradiated and that the Kienböck-Adamson technique [6,7] should be carefully applied by an experienced radiographer. Similarly, in America, Andrews [8] reported that over a period of twenty years 5000 cases had been successfully epilated in his clinic by unfiltered X rays without a single case of permanent baldness. Miedzinski and Lipski,[9] in Poland, use epilation by X rays in all patients with tinea capitis and they have noted no immediate or later side-effects; but the results of treatment were less successful in outpatients than inpatients. They attributed this to incomplete removal of infected hairs and inadequate application of fungicides. For tiny areas of ringworm, Beare [3] believes that the wearing of caps and exclusion from school is unnecessary since the fungus is spread via the stratum corneum into the hair follicle and then to the hair shaft, and the extrafollicular part of the hair cannot be infected directly. He attaches importance to the use of greasy fungicides to prevent the spread of the infection until spontaneous cure eventually takes place. Beare doubts whether any local applications, including chlorhexidine, are capable of curing *T. sulphureum* infections.

1. Walker, J. *Brit. J. Derm.* 1950, **62**, 239.
2. Partridge, B. G. *Trans. St. John's Hosp. derm. Soc., Lond.* 1952, p. 34.
3. Beare, J. M. *Brit. J. Derm.* 1956, **68**, 193.
4. Whittle, C. H. *Ibid*, p. 1.
5. Thorne, N. A., Grange, R. V. *Postgrad. med. J.* 1954, **30**, 423.
6. Kienböck, R. *Arch. Derm. Syph., Wien*, 1907, **83**, 77.
7. Adamson, H. G. *Lancet*, 1909, i, 1378.
8. Andrews, G. A. Diseases of the Skin. Philadelphia, 1946; p. 317.
9. Miedzinski, F., Lipski, J. *Brit. J. Derm.* 1956, **68**, 200.

HEADACHE AFTER SPINAL ANÆSTHESIA

ANÆSTHETISTS are sometimes reproached for not doing enough to investigate the sequels of spinal anæsthesia. This criticism, however, can hardly be applied to Vandam and Dripps, of the University of Pennsylvania, who have for several years been engaged in an exhaustive study of patients who have had spinal anæsthesia or a lumbar puncture. Their findings have been set out in several papers.[10–12] These do not include any major neurological complications, but they show very clearly the importance of minor sequels—most of which are troublesome and many incapacitating, though none is permanent. Vandam and Dripps's latest work [13] is concerned with headache, which is the commonest complication of spinal anæsthesia, and the disturbances of eye and ear with which it is occasionally associated.

In the series they studied, there were 8460 patients, who received 9277 spinal anæsthetics in the same hospital. For each anæsthetic a uniform technique was followed, except for the size of the lumbar-puncture needle, the type of local anæsthetic, and the occasional methods used to prolong the duration of anæsthesia, all of which were deliberately varied. The progress of the patients was carefully followed not only in the immediate postoperative period but also for from six months to five years later; and, in the final event, the outcome of about 89% of all the spinal anæsthetics could be analysed over a six-month period. At the same time 1000 patients who had had general anæsthesia for similar operations were used as controls and investigated in the same way.

Of those who had spinal anæsthesia, 11% had headache, 0·4% had eye symptoms, and 0·4% had ear trouble. Headache was most common in patients between 20 and 40; and it occurred twice as often in females as in males. This difference was largely explained by the large number of obstetric patients who had spinal anæsthesia for vaginal delivery; but even when these are excluded, headache still affected more women than men. The high incidence of headache after spinal anæsthesia in labour (22% in this series) is well known, and it is commonly attributed to the special factors present which can affect the pressure of the cerebrospinal fluid (C.S.F.). A low C.S.F. pressure seemed to be the cause of the headache after spinal anæsthesia. Perforation of the dura may leave a small hole through which fluid can escape. In Vandam and Dripps's series, needles varying from 16 to 24 gauge were used, and the incidence of headache was lowest when the smallest diameter was used. Moreover, with the smaller needles, when a headache did develop it was usually mild. Whenever a second lumbar puncture was performed after the onset of headache, the C.S.F. pressure was very low or unmeasurable; the pressure was never increased after spinal anæsthesia.

10. Dripps, R. D., Vandam, L. D. *J. Amer. med. Ass.* 1951, **147**, 1118.
11. Dripps, R. D., Vandam, L. D. *Ibid*, 1954, **156**, 1486.
12. Vandam, L. D., Dripps, R. D. *Surgery*, 1955, **38**, 463.
13. Vandam, L. D., Dripps, R. D. *J. Amer. med. Ass.* 1956, **161**, 586.

Similarly, Vandam and Dripps were able to relate both ocular and auditory symptoms to a decrease in intracranial C.S.F. pressure. With few exceptions these complications were associated with typical post-spinal-anæsthetic headache. Some lateral-rectus palsies followed the use of a large-bore (16 gauge) lumbar-puncture needle. Some patients' hearing was much impaired on measurement, and this might be explained by a fall in intralabyrinthine pressure, since the cochlear and subarachnoid space are connected anatomically.

Several other pieces of evidence from the survey support the idea of a syndrome due to decreased intracranial pressure after spinal anæsthesia; but no other cause, such as a particular local analgesic drug, could be identified. None of the complications was permanent, though some persisted for several months after anæsthesia; many caused considerable distress to the patients even when they did not last long. These facts, and the knowledge that sequels can be reduced in incidence and severity by proper precautions, are the chief lessons to be learnt from this investigation.

DIETETICS IN THE MODERN WORLD

ONLY eight special diets are necessary in clinical medicine, Dr. A. P. Meiklejohn declared in the opening paper at the International Congress of Dietetics in Rome on Sept. 10: a "fever" diet, low or high roughage, low fat, low calorie, low sodium, restricted carbohydrate, and high protein. Yet the task of adapting these to the individual patient's taste, needs, and circumstances was so time-consuming that a dietetic department required six dietitians for every physician. Dr. Meiklejohn emphasised the important and varied duties of the dietitian as an indispensable aid to the doctor: "male doctors may have a theoretical idea about calories, proteins, minerals, &c. . . . but how to translate these into terms of a meal that the patient will enjoy is something beyond their ken."

But the future of dietetics, he considered, lay in prevention rather than treatment. Our large measure of control over infectious disease had increased the urgency of the problem of feeding the world's growing population, and malnutrition was succeeding infection as man's greatest enemy (after himself, the cynic might add). Trophology, Dr. Meiklejohn's neologism for the science of nutrition, was thus coming into its own. Much more field work was needed, in which the dietitian had an important rôle to play, quite apart from the task of translating the scientist's recommendations into terms acceptable to the housewife and family in Pakistan, Poplar, or Peru. Inquiry into local feeding traditions might prevent the recurrence of such misadventures as the introduction into certain Pacific islands of kwashiorkor and calcium deficiency through the misguided encouragement of earlier weaning when there were no alternative sources of protein and calcium. Such an incident also pointed the way to a further field of research—the quest for nutritional supplements, such as cheap and easily produced sources of protein, minerals, and vitamins in or close to the areas where they are needed. When such supplements had been found and their supply arranged (often a complex undertaking involving the coöperation of many administrative departments—medical, agronomic, economic, and others), the next task facing the field dietitian was to persuade the people to use them to achieve a balanced diet, perhaps in the face of bitter opposition based on ignorance and prejudice.

In the socio-economic upheaval that accompanied the change from an agrarian to an industrial way of life, such as many parts of Africa and Asia were undergoing today, the dietitian had an important educational function, and her insight into the domestic aspects of nutrition might be a great help in answering questions of cause and effect. For new nutritional diseases were constantly being recorded, two outstanding examples in recent years being kwashiorkor and the syndromes which appeared in prisoners of war in the Far East.

Dr. Meiklejohn ended with words of welcome cheerfulness: "Do not let us be discouraged by dismal stories about the perilous present and doubtful future of mankind. They are fostered by loud-mouthed publicists who have lost faith in humanity through going about too much with people of their own kind. While they chatter together, a quiet unspectacular revolution is going on throughout the world—a gradual lifting of human nutritional standards from those of mere survival or insecure gluttony, to a new level of true nutritional health, both physical and mental."

ADENOVIRUSES

IN assessing the part played by the adenoviruses (formerly called A.D., A.P.C., R.I., or A.R.D. viruses [1]) in respiratory disease, important evidence has come from work on the effects of administering virus cultures to volunteers. In the first experiments of this kind adenoviruses of types 1 to 6 were given intranasally to volunteers [2]; there were very few clinical illnesses, although there was good laboratory evidence that infection had taken place. Later the same workers [3] described an attempt to measure the immunising activity of adenovirus vaccines. Vaccinated individuals and unvaccinated controls were challenged by swabbing a culture of type-3 adenovirus on the palpebral conjunctiva of one eye. About 300 infective doses of virus were inoculated, and this small amount of virus nevertheless produced an illness similar to the naturally occurring pharyngoconjunctival fever [4] in quite a high proportion of volunteers. When the sera taken from volunteers before inoculation were examined for neutralising antibody to type-3 adenovirus it was found that 28 out of 31 volunteers whose sera had no neutralising antibody developed definite illness, whereas only 14 out of 52 of those whose sera had neutralising antibody became ill. Ward et al.[5] have also reported that when adenoviruses of types 3 and 4 were swabbed on the conjunctiva and pharynx quite a high proportion of volunteers developed pharyngoconjunctival fever. Again, the frequency of illness was inversely related to the pre-existing neutralising-antibody titre.

On p. 592 this week Dr. Roden and his colleagues report the results of a similar study with type-1 adenovirus, which has not previously been tested in this way. The virus was administered intranasally to 11 volunteers, of whom 2 developed acute pharyngitis. Their illnesses resembled pharyngoconjunctival fever without conjunctivitis; the absence of conjunctivitis may have been due to the route of inoculation or to a difference in the behaviour of type-1 virus from types 3 and 4. The frequency of infection, as judged by laboratory evidence, was inversely related to the presence of pre-existing neutralising antibody in the volunteers' sera. We have very little knowledge of the significance of type-1 adenovirus in natural infections of man. Most of the strains have been recovered by culturing tonsils and adenoids removed from children at operation, and antibodies to type-1 virus seem to develop early in childhood.[2] Huebner et al.[3] mention work in progress which

1. See *Lancet*, 1956, i, 844.
2. Huebner, R. J., Rowe, W. P., Ward, T. G., Parrott, R. H., Bell, J. A. *New Engl. J. Med.* 1954, **251**, 1077.
3. Huebner, R. J., Bell, J. A., Rowe, W. P., Ward, T. G., Suskind, R. G., Hartley, J. W., Paffenbarger, R. S. *J. Amer. med. Ass.* 1955, **159**, 986.
4. Bell, J. A., Rowe, W. P., Engler, J. I., Parrott, R. H., Huebner, R. J. *Ibid*, 1955, **157**, 1083.
5. Ward, T. G., Huebner, R. J., Rowe, W. P., Ryan, R. W., Bell, J. A. *Science*, 1955, **122**, 1086.

shows that adenoviruses of types 1, 2, and 5 are associated with fever and pharyngitis in children, and details of this work will be welcome. One important question which volunteer experiments may help to answer is whether the different serotypes of adenoviruses are potentially capable of causing the same type of illness in susceptible individuals. It is possible that the differences found in the epidemiological patterns of the viruses of this group [1] may reflect differences in their distribution among age-groups of the population rather than basic differences in their capacity to cause disease in man.

AN ANTICONVULSANT FOR PSYCHOMOTOR EPILEPSY

PSYCHOMOTOR epilepsy remains resistant to medical treatment: any new drug which may be used to combat it is therefore welcome. Zimmerman [6] reports on the trial of a new substance N-methyl-αα-methylphenylsuccinimide ('Celontin') for this form of attack. He mentions 35 cases, but he does not give full information about the length of the trial or the time for which improvement was maintained. The findings must therefore be considered as preliminary ones. Zimmerman claims complete control of attacks in 7 cases and a reduction of 50% or more in 27 cases. So far no serious toxic effects have been noted, and the drug seems to be to some extent effective against grand mal and petit mal as well. Indeed, its action in psychomotor attacks was first noted incidentally during an investigation of its effect on petit mal. In view of these findings, further results will be awaited with interest.

NICKEL DERMATITIS

ABOUT 10% of outpatients in the skin department of a general hospital have some form of contact dermatitis. Many of the conditions are caused by direct irritants, but with diligence a high proportion of dermatitis due to specific contact sensitisation may be detected. Calnan [7] has shown that 40% of patch-test-positive cases are due to nickel. But this figure is probably artificially high; for one thing, nickel dermatitis is often readily diagnosed by an experienced observer, who then applies the appropriate test; and, moreover, there are examples of undoubted contact sensitisation in which the specific cause is completely elusive, so that no positive reaction is ever recorded.

Calnan studied 400 women, in 95% of whom stocking-suspender dermatitis was the first sign of nickel sensitivity. Such patients rarely sought medical advice before the dermatitis had spread to secondary areas not in direct contact with nickel. The bend of the elbow was a common secondary site, and the patient did not often associate it in her mind with the primary patches on the thighs. Other non-eczematous forms of dissemination were noted, such as erythema multiforme, urticaria, or generalised pruritus. Calnan reported dissemination in no less than three-quarters of this series—a much higher figure than in other kinds of contact dermatitis. Dissemination is of particular importance both practically and theoretically, since the secondary lesions may persist after the initial foci have disappeared. Calnan believes that suspender dermatitis is only rarely caused by something other than nickel sensitivity—or more specifically that friction, trauma, and allergy to rubber are seldom responsible. Moreover, in his experience nickel sensitivity is permanent in the sense that patients remain patch-test-positive. He admits that not all areas in contact with nickel-plated articles show an eczematous response in nickel-sensitive patients and he has seen cases in which the common "secondary" sites are involved before those areas in contact with the metal. About 30% of his patients showed some other variety of dermatitis, but in the vast majority nickel dermatitis preceded any other lesion. Eczema of the hands was present in no less than 20% of his 400 cases, and others had eruptions resembling such conditions as seborrhœic dermatitis and nummular eczema.

Wells [8] demonstrated that nickel passes into solution from a nickel coin or nickel-plated article if these are placed in synthetic sweat concocted from $^1/_2$% sodium chloride, $^1/_2$% urea, and $^1/_4$% lactic acid in water. He showed that nickel has a strong affinity for keratin, which will take up the metal from solutions containing as little as 1 part of nickel per million. He also observed that a positive patch test could be elicited in a nickel-sensitive patient with a nickel coin placed in contact with the skin for no more than an hour. It is clear that infinitesimal quantities of the allergen may be involved in producing, or at any rate provoking, nickel dermatitis. In everyday life it is almost impossible to avoid some contact with nickel even if more obvious sources are removed. It is therefore conceivable that some persistent forms of dermatitis are due to inadvertent contact with the metal. Cross-sensitivity to other metals is known to occur sometimes; cobalt is unlikely to be of practical consequence except in industry, but sensitivity to copper, noted by Calnan in 3 of 22 cases, is more generally relevant. Contact sensitivity to other unrelated substances, such as plants, cosmetics, or dyes, may also accompany nickel dermatitis. Instances of this multiple sensitivity are probably relatively uncommon, so that some observers attribute relapse or chronicity to purely non-specific factors such as trauma, friction, infection, and minor primary irritants. Wilson [9] thinks that emotional stress is prominent in provoking relapses of nickel dermatitis, and he suggests that those who are constitutionally prone to this particular type of neurodermatitis are also abnormally susceptible to dermatitis from nickel contact.

Morgan [10] reported that 43% of his patients became insensitive to nickel by patch test, but that, in spite of this loss of sensitivity, many of them still had eczema. He felt that the demonstrable nickel sensitivity was "a transitory phase in the course of a series of eczematous reactions"—which seems to imply that it was symptomatic rather than a cause of the disease. Others are in sympathy with this view and believe that some patients develop contact dermatitis because they are on the verge of an explosion of neurodermatitis. These critics will point to the appearance of lesions in the "secondary" sites before there is dermatitis in the nickel-bearing areas, to the persistence of disseminate lesions even when the patient is confined to bed in hospital out of all apparent contact with nickel or primary noxæ, and to instances in which women who have recovered from nickel dermatitis have been able to wear metal suspenders again with impunity. If this is the explanation it is curious that nickel should be the detonator in such a high proportion of cases, that multiple sensitivities should not be more common, and that dermatitis unprovoked by physical factors should so rarely precede nickel dermatitis.

We know very little about what predisposes to contact sensitisation and no more about the mechanism of dissemination and perpetuation. The whole subject of contact dermatitis, apparently so obvious, abounds in fact with beguiling mysteries. Nickel dermatitis seems to offer a particularly useful opportunity for studying these problems of wider significance, and the British work to which we have referred should contribute much to our knowledge and understanding of these matters.

6. Zimmerman, F. T. *Arch. Neurol. Psychiat.* 1956, **76**, 65.
7. Calnan, C. D. *Brit. J. Derm.* 1956, **68**, 229.
8. Wells, G. C. *Ibid*, p. 237.
9. Wilson, H. T. H. *Practitioner*, 1956, **177**, 303.
10. Morgan, J. K. *Brit. J. Derm.* 1953, **65**, 84.

Special Articles

THE PHASES OF HUMAN GAIT*

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THERE have been many elaborate surveys of normal gait—e.g., those of Elftman (1934), Schwartz et al. (1934), and Morton (1935)—but the variations in foot structure that help to give each of us a characteristic style of walking merit further study.

With the aid of a new type of pedograph that gives quantitative results the functions of the foot during walking have been studied in young adults. All were symptom-free and may legitimately be described as "normal" subjects, even though the shape of their feet and the way they walked did not necessarily conform to preconceived ideas of normality.

100 white medical students aged 17–25, including 12 women, coöperated in this investigation. Radiographs of their feet were obtained by the standard procedure of Hardy and Clapham (1951), and the prints left when they walked with powdered feet upon a black floor were measured. In addition 26 students were investigated with a plastic pedograph.

By means of this apparatus photographs are obtained, at intervals of $^1/_{30}$ sec., that show the profile of the foot and ankle, together with a view of the sole of the foot. Across the sole appear horizontal black bands whose width at any point is an index of the pressure borne by that part of the foot at that moment. The underlying principles of the apparatus have previously been described (Barnett 1954).

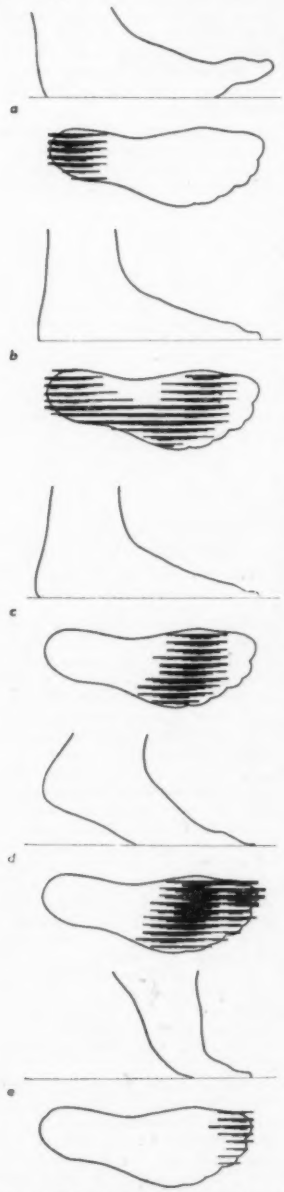

Fig. 1—Pedograph records showing the five phases of stance period.

Normal Gait

From a study of pedograph records it is apparent that, in normal gait, the period during which the foot makes contact with the ground (the stance period) can be divided into five phases: (1) the heel phase, (2) the standing phase, (3) the metatarsal phase, (4) the forefoot phase, and (5) the step-off phase.

Heel Phase

For the first 15–20% of the stance period the heel alone is in contact with the ground. The posterolateral part of the heel makes initial contact; the main reason for this is that the swinging foot, held in the position of rest at the subtalar joint, is slightly inverted. The whole heel very soon bears weight evenly, however (fig. 1*a*).

Standing Phase

In this phase pressure is taken by the heel, the outer side of the sole, and the heads of the metatarsal bones (fig. 1*b*). It lasts for about 30–35% of the total stance period and represents the phase during which the centre of gravity of the body is directly above the foot concerned. The pressure distribution is therefore very similar to that obtained during standing (fig. 2).

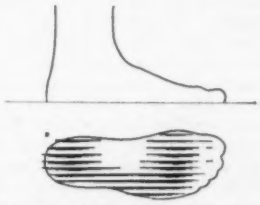

Fig. 2—Pedograph record during standing.

The pattern of weight-bearing indicated by the pedograph during standing, or in the standing phase of walking, is remarkably constant, apart from variations in the relative pressures beneath the individual metatarsal heads. This finding is difficult to reconcile with the statements made by many authorities. In fig. 3 four differing theories about the form of the normal foot are shown diagrammatically, together with the pedograph record that each would be expected to give.

Bankart (1935) believes that the perfect foot collapses completely when bearing weight, with the result that the arches disappear. No pedograph record indicating this subsidence of the arches has been obtained. There does not seem to be any evidence that the symptomless European foot behaves like this, and Bankart's view that people of other races who do not wear shoes have feet whose arches disappear when bearing the body-weight does not accord with the careful work of James (1939) on the feet of natives of the Solomon Islands.

At the other extreme Dickson and Diveley (1953) consider that the foot has three permanent arches: a medial longitudinal arch, a lateral longitudinal arch, and an anterior transverse arch. Again, no foot in which three distinct arches can be made out has been observed; nor is there any evidence from pedograph records to support the view that, in standing, "such weight as falls on the forefoot is borne by the first and fifth metatarsal heads" (Stamm 1955), the forefoot being arched transversely until the heel is raised from the ground.

Morton (1935) believes that the foot bears two longitudinal arches: a high medial and a lower lateral.

Ellis (1889), supported by Wood Jones (1944) and McKenzie (1955), thought that the normal foot resembled a half-dome,

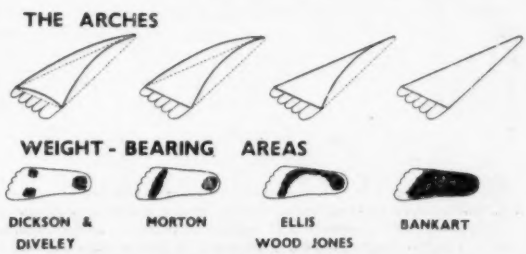

Fig. 3—Four theories of architecture of normal foot.

* Based on a paper read before the St. Thomas's Hospital Research Club, May, 1955.

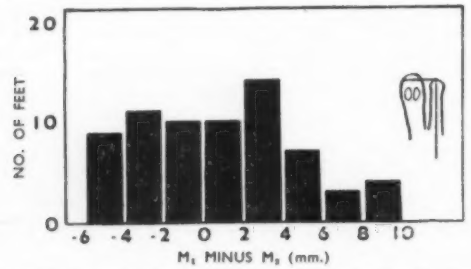

Fig. 4—Relative protrusion of first metatarsal in present series, assessed by Morton's method.

with the heel, the outer side of the sole, and the heads of the metatarsals all in contact with the ground, and the inner border raised.

Pedograph records suggest that the European foot has a form intermediate between Morton's and Ellis's concepts. When the foot is not bearing weight, the lateral longitudinal arch certainly exists. When the foot is bearing the weight of the body the arch sinks, with the result that the skin normally touches the ground. The arch does not flatten completely, and if one walks barefoot on flat hard ground the lateral border of the foot virtually takes no share of the body-weight. This would be equally true in the shod foot if the sole of the shoe were flat and unyielding; but on soft ground, a heavy pile carpet, or the slightly resilient surface of the plastic pedograph the lateral side of the foot does bear an appreciable share of the weight, and Ellis's analogy of the half-dome is apt. Possibly our feet would be even more like a half-dome and less like Morton's concept if we had never worn shoes, but the effects of footwear on the shape of the foot are beyond the scope of the present paper.

Metatarsal Phase

This phase, in which all the weight is borne by the metatarsal heads (fig. 1*c*), seldom exceeds 10% of the stance period. Occasionally it is absent as an independent phase, the toes beginning to take some share of the body-weight before the heel has left the ground. Nevertheless it is an important phase, the downward force being concentrated on a very small area, and the pressure therefore being very great.

Morton's theory of gait needs mention here. Believing that in the normal foot the first and second metatarsals protrude to an equal extent, Morton claims that in the later phases of gait the foot is levered forward about an axis that passes transversely through the heads of these two bones. If the first metatarsal is unusually short, the head of the second bears too great a share of the burden of weight-bearing, eventually giving rise to pain on walking. This ingenious theory does not seem to have wide support in this country, but some authorities—e.g., Lake (1952)—apparently accept it. Harris and Beath (1952), in particular, do not agree that a short first metatarsal is a cause of painful feet.

A fallacy in Morton's theory was pointed out by Wood Jones (1944), who stated that, far from being an atavistic defect, a first metatarsal that does not protrude so far as the second is the usual finding in normal feet. Analysis of 130 feet from cadavers and 300 radiographs of the feet of healthy young adults supports this contention (Barnett and Napier 1953), the so-called "short first metatarsal" occurring in about 50% of the total. In 30 of the 68 people in the present study in whom this feature was examined the head of the first metatarsal fell short of the second (fig. 4).

Several factors can influence the effective length of one metatarsal relative to another. As Morton has emphasised, if the pair of sesamoid bones beneath the head of the first metatarsal are placed unusually far back, the result is to shorten the effective length of this metatarsal. Again, the compressibility of the tissues beneath the bones differs. When the first metatarsal head is forced downwards, there can be little reduction in its distance from the ground, because the sesamoids are incompressible and the thickness of soft tissue is small. Experiment shows, however, that the relatively thick soft tissues beneath the second metatarsal head can be diminished by about 2 mm. when a weight of 4 kg. is applied vertically here. In theory these factors should be taken into account, but it was decided that, in attempting to verify or disprove Morton's theory, his own method of measuring the metatarsal protrusion should be used. Accordingly the distance that the tip of the first metatarsal was in advance of a line passing through the tip of the second, drawn at right angles to the second metatarsal shaft—Morton's own method—was measured in 26 people, and these figures were compared with the maximal pressure borne by the first and second metatarsal heads, determined from pedograph records.

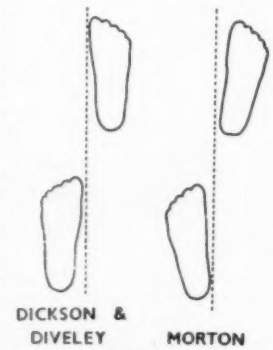

Fig. 6—Two theories about the normal angle of gait.

The results are shown in fig. 5. It can be seen that the black columns (pressure beneath the first metatarsal) increase in height as the relative protrusion of the first metatarsal increases, but there is no corresponding change in the height of the white columns (pressure beneath the second metatarsal). In other words, the more the first metatarsal protrudes beyond the second the greater is its share of the total load. In feet where the first metatarsal is "short," however, the pressure is well distributed across the other metatarsal and does not exceed 4 kg. per sq. cm. beneath the second metatarsal, presumably because other factors can compensate for the normal degree of protrusion of this bone.

In ordinary walking the pressure beneath the second metatarsal head could be decreased relative to the first in several ways. Only two will be considered here: (1) walking with the toes turned out and (2) extending the interphalangeal joint of the great toe instead of the metatarsophalangeal joint.

The normal angle of gait is, rather surprisingly, a subject of dispute. Fig. 6 shows versions taken from standard works. Admittedly, training by parents, teachers, and physical-

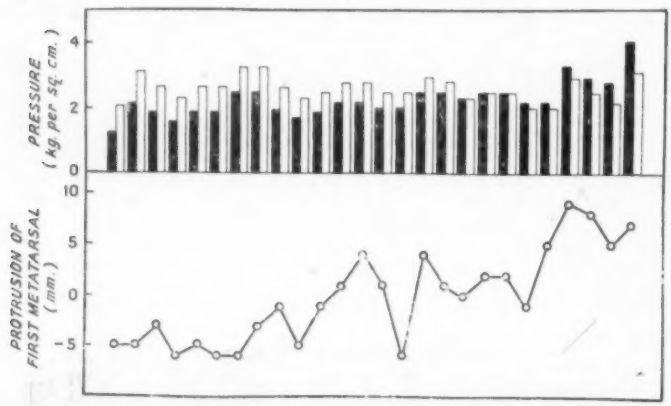

Fig. 5—Pressures reached beneath heads of first metatarsal (black column) and second metatarsal (white column) in 26 people; share borne by first metatarsal increases from left to right. Corresponding protrusion of first metatarsal beyond second is shown graphically below.

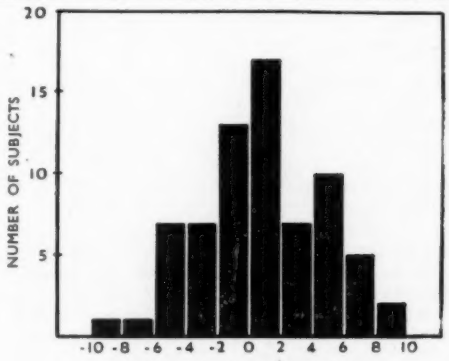

Fig. 7—Angle of gait in present series.

training instructors may help to determine whether we walk with toes turned in or out, but Morton's (1932) studies of African natives as well as of American students are sufficiently in agreement to suggest that there is a normal mean, independent of fashion. The commonest angle of gait, which is defined as the angle between the medial side of the foot and the direction of walking, is about 7°. (In the present small series, the mean angle of gait in the 70 students examined [fig. 7] was somewhat lower than Morton's figures.) We may reasonably assume that most people find that if they turn their toes out slightly they walk without discomfort: the reader can readily prove to himself, by walking a hundred yards with the feet pointing in an unaccustomed direction, that an unusual angle of gait can cause pain. It is tempting to postulate an "average" person who has a first metatarsal that falls a few millimetres short of the second and habitually walks with his toes turned out slightly. The discrepancy between Morton's theory and the observation that the line joining the heads of the first two metatarsals is not usually transversely oriented within the foot would then disappear, for out-turning of the foot would make this line perpendicular to the direction of progress. The present series, however, is not large enough to allow this hypothesis to be substantiated.

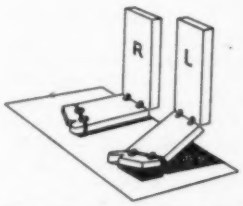

Fig. 8—Wooden models of feet (see text).

The second possible method of compensating for a relatively short first metatarsal (extension of the interphalangeal joint of the hallux while the metatarsophalangeal joint is kept almost immobile) was noted in only 3 students, but less obvious examples may well have been missed. The result of this type of mobility is that the effective length of the first metatarsal is increased by the length of the proximal phalanx—the two bones move almost as one, hingeing at the interphalangeal joint. This movement should not be confused with premature and unusually forceful flexion of the hallux as a whole, which sometimes relieves the metatarsal heads of some of the burden of weight-bearing (Harris and Beath 1952).

The possibility was considered that inversion or eversion movements at the subtalar joint could compensate for first or second metatarsals of unusual length. There is experimental evidence that this joint plays little part in normal walking (Close and Inman 1953), and this is supported by the fact that patients with subtalar arthrodesis commonly walk in a way that does not differ perceptibly from the normal. Subtalar movements may be of importance in certain unusual gaits, however (McKenzie 1953).

Forefoot Phase

During this phase, which occupies about 30% of the stance period, both the toes and the heads of the metatarsals are bearing weight (fig. 1*d*). Although the hallux usually predominates, the pedograph records show that the other toes, especially the second, share a considerable part of the total load.

If Morton's theory that the foot is levered forwards at the first and second metatarsal heads is valid, it is remarkable that the outer metatarsal heads can bear any part of the total pressure during the last phases of walking. The foot is becoming more and more vertical; so the 3rd, 4th, and 5th metatarsals, which hardly ever protrude as far as the second, would be expected to rise further from the ground. The observation, in all the pedograph records, that in practice these bones continue to play a considerable part in weight-bearing during the forefoot phase may depend on the fact that in this phase the foot is being actively plantar-flexed at the ankle-joint.

It can be shown experimentally that the axis of rotation at the ankle is not "transverse," as is commonly stated. Unless the foot is near the neutral position, the axis is inclined (Barnett and Napier 1952); of more relevance to the present study is the fact that the axis is not at right-angles to the long axis of the foot but points backwards and laterally (Barnett 1953, Hicks 1953). This oblique axis may usefully be regarded as lying almost parallel to the heads of the outer four metatarsals.

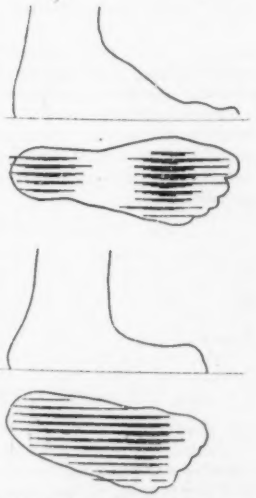

Fig. 9—Pedograph records from two patients whose feet appeared flat (see text).

Now, if wooden models of the leg and foot are made in which the ankle and metatarsophalangeal joints are represented by carpenter's hinges, the significance of having parallel hinges becomes apparent. If the ankle hinge is made "transverse," the outer side of the forefoot is raised from the ground as soon as the ankle is plantar-flexed (fig. 8). When the two hinges are made parallel, however, the outer part of the forefoot remains in contact with the ground.

De Palma (1955) maintains that the outward torsion of the lower end of the tibia—responsible for the obliquity of the ankle axis—is a characteristic feature of the human limb. It is therefore likely that the obliquity of the ankle axis in man is related to bipedalism, and the suggestion that the distribution of pressure across the whole forefoot is thus facilitated may explain this relationship.

In some people the forefoot phase is not clearly demarcated from the preceding ones, for the toes begin to exert pressure on the ground before the heel has left it. This may be an abnormal phenomenon, however, seen only in people who are not accustomed to walking without shoes. On soft yielding ground or on slippery surfaces this premature toe function is probably a normal mechanism ensuring that the area of foot contact never falls below that required for stability.

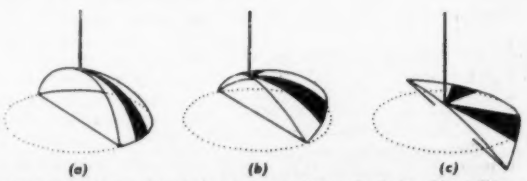

Fig. 10—Half-dome (*a*) made to appear flatter by being tilted (*b*) or being crushed (*c*).

Step-off Phase

During this final phase, which usually occupies 3–10% of the stance period, the pressure is borne entirely by the toes, especially the hallux (fig. 1*e*). The amount of pressure is small, the other foot by this stage bearing most of the body-weight. The impression of all five toes is normally seen. Lambrinudi (1938) stated: "Given freedom the little toe is a very valuable organ," and certainly it plays a greater part in the step-off phase than might have been expected.

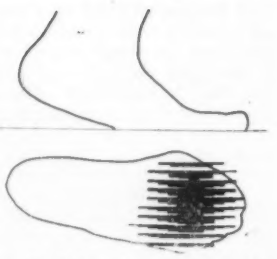

Fig. 11—Pedograph record showing excessive pressure beneath second metatarsal head.

Abnormal Gait

Division of the stance period of gait into five phases is of value not only in analysing normal gait but also in the study of patients with symptoms of pain or discomfort in the feet. A few examples of disordered gait in patients with foot disorders will be described, to illustrate the value of analysis of gait into five phases.

Heel Phase

As might be expected from a consideration of the excellent results that may follow a well-performed Syme's amputation, the tissues of the heel can bear the body-weight for an unusually large proportion of the total stance period without ill effects. In one patient with a fixed calcaneus deformity the heel was the only weight-bearing region for more than 80% of the stance period, yet there was no evidence of this excessive load except a hard painless thickening of the underlying skin.

Standing Phase

Although the distribution of pressure during the standing phase is remarkably uniform in normal people, this is the commonest phase to show abnormalities in patients complaining of painful feet. Fig. 9 shows the pedograph records in 2 patients, both of whom had been sent to the outpatient department with a diagnosis of "flat-feet." On clinical examination both indeed appeared to have a medial longitudinal arch flatter than usual. Ellis's analogy of the half-dome is helpful here. A half-dome can be made to appear flatter, viewed from the side, either by tilting it or by crushing it flat, as shown in fig. 10. In the first patient the foot had tilted (a valgus or pronated-foot disability), and the lateral side of the foot necessarily rose from the ground, a fact which was not realised until the pedograph records were examined. In the second patient the half-dome had collapsed, and the whole flattened foot bore the body-weight as in Bankart's "ideal" foot. Obviously it would be impossible to produce such a disorder unless ligaments were stretched, and no amount of muscle exercises could be expected to reconstitute the lost arch in such a foot. Possibly the observation in a patient that the lateral border of the foot is raised may be of prognostic value, for it occurs only in a valgus disability uncomplicated by true flattening of the foot.

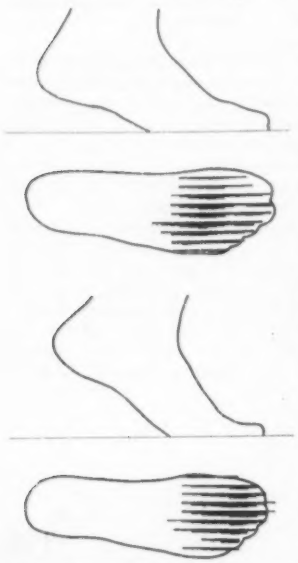

Fig. 12—Pedograph records after surgical treatment of hallux valgus (see text). Upper record (of left foot) has been reversed for ease of comparison.

Metatarsal Phase

It is to be expected that second metatarsals which protrude to an exceptional extent will bear an abnormal burden, as Morton suggests, because the compensating mechanisms described above would be inadequate. The pedograph record from a patient with pain under the second metatarsal head is shown in fig. 11; a radiograph showed that the second metatarsal protruded 11 mm. beyond the first. The importance of an excessively long second metatarsal as a cause of pain under the forefoot is not easy to judge, but since it is readily diagnosed by taking an ordinary dorsiplantar radiograph and responds well to measures designed to relieve the metatarsal of its abnormal burden (Morton 1939) it is a condition to be borne in mind.

More common as a cause of pain under the forefoot is the undue prolongation of the metatarsal phase. In patients the duration may be increased, from the usual maximum of 10%, to 50% of the stance period. This change is usually seen in patients with a high longitudinal arch and clawed toes, and the prolongation of the phase is due to tardy use of the toes (see below).

Forefoot and Step-off Phases

These two phases may be considered together for the sake of brevity. The most common defect at this final stage of gait is delayed or inadequate function of the toes. As a result the metatarsal phase is prolonged, as described above, and the step-off phase may be absent, the metatarsal heads and the phalanges being lifted simultaneously from the ground.

Inadequate function of the toes is not necessarily detected by ordinary clinical tests, for these patients may be able actively to plantar-flex their toes, and no pathological clawing may be present. It is likely that this condition, which may be termed "masked clawing" of the toes and is presumably due to habitual disuse of the interosseus and lumbrical muscles, must be associated with added strain on the metatarsal heads. Lack of toe function in walking (as distinct from truly non-functional toes) should be considered as a possible cause of metatarsalgia in a foot that appears normal on clinical examination.

The type of great-toe movement in which the first metatarsophalangeal joint is kept relatively immobile while the interphalangeal joint is freely dorsiflexed has obvious disadvantages, even in feet where it compensates for a very short first metatarsal. In particular, the terminal articular surface on the first metatarsal must be pressed with abnormal force against the base of the proximal phalanx. Bingold and Collins (1950) have shown that this type of movement is seen in patients with hallux rigidus, and it is perhaps worth recording that, in one patient with hallux rigidus on the right side, dorsiflexion of the great toe on the symptomless foot took place mainly at the interphalangeal joint rather than the metatarsophalangeal joint. Nilsonne (1930) pointed out that in most patients with hallux rigidus the first metatarsal protrudes beyond the second. It is probably necessary to distinguish those people who have this unusual toe mobility in compensation for a short first metatarsal from those exhibiting the same type of gait but whose first metatarsals are of adequate length. The second group would be much more likely to develop painful hallux rigidus.

Analysis of gait has its place in the follow-up of patients after operations on the foot. For example, persistence of symptoms after surgical treatment of hallux valgus may be due to a non-functional great toe, with a consequent added strain on the other toes and the metatarsal head region. The pedograph records in fig. 12 correspond to the two feet of a woman who underwent bilateral treatment for hallux valgus: the Mayo procedure on the left and an arthrodesis of the first metatarsophalangeal joint on the right. It can be seen that the great toe is functionless on the left side. A similar defect has been observed in 4 other patients complaining of pain recurring after the Mayo operation.

The temporal analysis of gait by pedography is essential for the full understanding of normal and abnormal wear of boots and shoes. By comparing the shoes of patients who had an abnormal gait with the corresponding pedograph records, it has been possible to assess minor abnormalities in the wear of soles, heels and uppers, and the worth of toe-raising springs and similar appliances.

Conclusion

A pedograph that involves kinematography, even the relatively simple device of Elftman (1934), is unsuitable for routine use in the outpatient clinic. Nevertheless it is invaluable for research, yielding information that is unobtainable by any other means.

I wish to thank Prof. George Perkins and the staff of the orthopædic department of St. Thomas's Hospital for allowing me to examine many of their patients; Mr. C. V. Hardwick and Mr. A. L. Wooding for radiographic and photographic work; Prof. D. V. Davies for helpful criticism and advice; and the students and patients who coöperated in this study.

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"Some indeed suggest . . . that the general practitioner now has so many effective drugs at his disposal, especially for the treatment of acutely ill patients, that he seldom thinks of calling in the physician to advise him or stand behind him when his patients have the pneumonia or meningitis or (a few years earlier) pernicious anæmia that would once have threatened them with death. On the other hand, the surgeon has invaded the thoracic, cardiac, neurological and other fields to such effect that often he likes to attend himself to much of the diagnosis and general management as well as to the operative surgery that once was practically his delimited territory. By the time the patients regarded as having psychosomatic disorders are packed off to the psychiatrist, the physician is left with a handful of patients presenting insoluble diagnostic problems and untreatable chronic complaints, none of which are likely to lend lustre to his reputation or fatness to his pocket book."—*Med. J. Aust.* Sept. 8, 1956, p. 385.

SILICONE-RUBBER TUBING IN BLOOD-TRANSFUSION WORK

CLINICAL TRIALS

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BLOOD-TRANSFUSION practice in the United Kingdom usually involves the repeated use of the same equipment. Ideally the tubing used for this purpose should therefore be inert, non-toxic, resistant to repeated sterilisations by autoclaving, and if possible transparent. Silicone rubber closely approaches these requirements. The work described below consisted in clinical trials undertaken to determine the suitability of silicone-rubber tubing for blood-transfusions and to compare the properties of several compositions.

There have been reports that certain types of natural rubber tubing give rise to non-pyrogenic reactions when the tubing is used for intravenous infusion of solutions into the body; but, in the absence of any definite information on the identity of the toxic component or any convincing explanation of the mechanism of its action, no definite conclusions can be drawn from the published observations.

Stokes and Busman (1920) reported that a certain brand of so-called pure gum-rubber tubing contained, when new, a toxic agent responsible for reactions following intravenous injection of arsphenamine and possibly also of alkaline solutions and other transfusion media. It was confirmed by Busman (1920) that the same tubings gave reactions in blood-transfusion work. The identity of the toxic component was not established.

In an investigation of the causes of thrombophlebitis following intravenous infusions through natural rubber (latex) tubing, the importance of the duration of the infusions was established, but no evidence of the presence of toxic products in the tubing was presented (Bolton Carter 1951). It was shown, however, by Handfield-Jones and Lewis (1952) that the incidence of infusion thrombophlebitis could be correlated with the sample of natural rubber tubing concerned.

In 21 transfusions through silicone rubber, reported by Fletcher (1956), no local or general adverse reaction took place.

The silicones, or organopolysiloxanes, comprise a group of polymers containing silicon, oxygen, and organic groupings. When linear polymers of the type shown in fig. 1, of high molecular weight, are filled with reinforcing

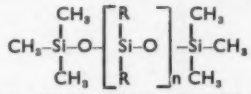

Fig. 1—Linear silicone polymer, where R is usually CH_3.

fillers, such as finely divided synthetic silicas and diatomaceous earths, and vulcanised in the presence of an oxidising catalyst, such as benzoyl peroxide, an elastic product known as a silicone elastomer or rubber is obtained. These rubbers are distinguished by their resistance to high temperatures and by retention of flexibility at low temperatures, beyond the limits of other synthetic or natural rubbers.

A detailed review of the methods of preparation, properties, and applications of silicone rubbers, including references to earlier work, has been published by McGregor (1954). The properties of a particular rubber depend on, among other factors, the composition and molecular weight of the organosiloxane polymer on which it is based, as well as on the nature of the filler and catalyst and the conditions of vulcanisation. Since these factors may influence the suitability of silicone rubbers for use in blood-transfusion equipment, representative rubbers were examined in clinical trials. Certain fillers, such as a silica aerogel, impart high water-absorption to rubbers containing them, whereas rubbers filled with, for example, an amorphous precipitated silica or a pyrogenic silica are characterised by their low water-absorption. Since both natural and silicone rubbers with relatively high absorptive capacities also readily absorb blood, this may be an important factor in determining suitability for blood-transfusion purposes. It should be realised that silicone polymer cannot be used alone, because the incorporation of a filler is necessary to give it body and to make it processable.

The silicone polymers—i.e., unfilled organopolysiloxanes—are characterised by their physiological inertness and very low toxicity in contact with the skin or when ingested or injected by the intraperitoneal and intradermal routes (Rowe et al. 1948). Similar observations have been reported by Barondes et al. (1950). The toxicity of silicone rubber to animal tissues has been compared with that of catgut, cotton, polyethylene, and polyvinyl polymers. The silicone showed the least reaction (Gale et al. 1952). Brudenell (1954) studied the resistance of silicone rubber to fungi, such as *Aspergillus niger* and *Penicillium citreum*; the moulds grew on natural rubber but not on silicone rubber under comparable conditions.

The suitability of silicone rubber for tissue-culture has been demonstrated by MacDougall (1953), who showed that rate of growth and other properties of typical chick-embryo-tissue explants were unaffected by the presence of silicone rubbers. Coating of glassware and hypodermic needles with a thin layer of silicone polymer has been suggested as a method for delaying the coagulation of blood in contact with the surface (Jacques et al. 1946).

Fig. 2—Construction of transfusion sets. Bottle on right contains saline solution.

Experimental

Clinical Trials of Silicone Rubber in Transfusions of Blood and Serum

Seven transfusion sets were made up, each with one of seven different types of silicone-rubber tubing. The sets were identified by means of 1-inch lengths of coloured silicone-rubber tubing. In the data which follow the various sets are identified by the same colour codes. The construction of the transfusion set is shown in fig. 2.

The procedure for sterilisation followed standard practice. The various parts of the set were wrapped in lint, and each set was enclosed inside a separate stainless-steel sterilising container, which had the usual perforations to allow ingress of steam during sterilisation. The sterilisation was done in a Hawkins steam steriliser at a pressure of 15 lb. per sq. inch for thirty minutes.

These marked transfusion sets were used continuously from Jan. 3, 1955, until they showed signs of deterioration, when they were finally withdrawn for physical and chemical examination. Transfusions given were packed red cells (1–2 pints) on 273 occasions, serum 11 times to patients with Christmas disease, and fresh donor's blood 12 times to hæmophiliacs. The blood-transfusions lasted two to four hours.

The patients receiving the 273 transfusions in the main group were all very ill—with leukæmias, Hodgkin's disease, aplastic anæmia, myelomatosis, hæmolytic anæmia, or severe bleedings from œsophageal varices—and were under the care of one of us (J. F. W.). The transfusions were given both to inpatients in the Manchester Royal Infirmary and to outpatients in the departmental transfusion clinic by the medical staff of the department of hæmatology, with the assistance of Sister B. Poole, S.R.N., S.C.M., and Mr. S. Coxon, chief technician, who supervised the patients and the preparation and sterilisation of the sets.

Many of the patients received multiple transfusions over the whole period, and the 3 rigors reported did not recur in the patients during subsequent transfusions with the same sets.

Composition and Some Properties of Silicone-rubber Samples

The compositions of the silicone rubbers used in this work are summarised in table I in terms of nature of the siloxane polymer, filler, catalyst, &c. The rubbers were compounded in the normal way, extruded into tubular form ($^3/_{16}$ inch internal diameter, $^5/_{16}$ inch external diameter) and cured.

Data on the water-absorption of the rubbers are included in the table. Specimens of the rubber tubings (10–15 g.) were immersed in distilled water at 100°C for eighteen hours (three periods of six hours on successive days). Little further increase of weight took place under these conditions after twelve hours' immersion. The results are expressed as percentage increase of weight, and it has been assumed that this is due to water-absorption. Specimens of tubing containing a silica aerogel as filler and similar in composition to the tubing with red colour code (table I) absorbed relatively large amounts of citrated blood. Samples of the rubber were immersed in citrated blood (preserved by addition of 0·5% solution of sodium ethyl mercurithiosalicylate [thiomersal, 'Merthiolate']) at 18°C. At intervals the rubber was removed, rinsed free from blood with saline solution, dried with filter-paper, and weighed. The increases in weight were 3, 4·4, and 5·5% after 66, 90, and 114 hours' immersion respectively.

The presence of blood residues in silicone-rubber tubing as well as natural rubber tubing used for two or more transfusions was confirmed by means of the benzidine test. A sample of tubing about 0·5 inch long, after being washed and autoclaved in the usual way, was opened along its longitudinal axis and secured with pins to a piece of cork. One drop of benzidine solution (0·2% in glacial acetic acid) was placed in contact with the tube, followed by a drop of 3% hydrogen-peroxide solution. A deep blue developed which faded after a few minutes. The test was weakly positive after 2 transfusions and definitely positive after 5 or more. Unused tubing gave a negative reaction. The presence of blood residues in specimens of silicone-rubber tubing after 15 transfusions was confirmed by Kjeldahl nitrogen

TABLE I—COMPOSITION AND PROPERTIES OF SILICONE RUBBERS

Colour code	Composition of rubber						Water absorption after 18hr. at 100°C (%)
	Polysiloxane gum		Filler		Benzoyl peroxide (pts. by wt.)	Additive (pts. by wt.)	
	Type *	Parts by wt.	Type	Parts by wt.			
Orange	Dimethylpolysiloxane (E. 300)	100	Amorphous precipitated silica	45	3·3	Nil	0·45
Black	Methylphenylpolysiloxane (E. 350)	100	Amorphous precipitated silica	45	3·3	Nil	0·27
White	Dimethylpolysiloxane (E. 301)	100	Amorphous precipitated silica	45	3·3	Nil	0·39
Red	Dimethylpolysiloxane (E.301)	100	Silica aerogel	45	3·3	Nil	12·0
Green	Commercial silicone rubber of unpublished composition						0·34
Yellow	Dimethylpolysiloxane (E. 300)	100	Pyrogenic silica	35	3·0	2·5	1·2
Blue	Methylphenylpolysiloxane (E. 350)	100	Pyrogenic silica	35	3·0	2·5	0·59

* The reference numbers in this column are to elastomeric gums marketed by Imperial Chemical Industries Ltd.

determination. The tubing contained 0·065% nitrogen, compared with 0·015% in the unused controls. On the basis of a value of 3·0–3·7% as the total nitrogen content of human blood (Harrow 1941) the difference, 0·05%, corresponds to the presence of approximately 1·5% of blood in the tubing. There was no correlation between the presence of blood residues in the tube and the three reactions noted during transfusions (table II).

Properties of Silicone-rubber Tubing after Repeated Use for Transfusions

At the conclusion of the clinical trials the tubings were returned to the laboratory for examination. The most important properties which influence their suitability for blood-transfusion work are summarised below:

Colour code orange.—This set was withdrawn from service, after 45 transfusions, because traces of blood began to seep through the walls of the tubing. Subsequent examination revealed the presence of three fine "pin-holes" in the wall through which the blood had leaked. In other respects the rubber was in good condition. It was still firm, with little signs of tackiness. It had softened slightly and was darker.

Colour code black.—Withdrawn after 34 transfusions, the rubber was tacky both inside and out, with a tendency for particles to break away from the interior surface.

Colour code white.—This set was withdrawn, after 44 transfusions, for the same reasons as "orange." There were two fine "pin-holes" in the wall of the tubing. In other respects the tubing was satisfactory, being only slightly tacky and a little softer.

Colour code red.—After 33 transfusions the tubing was withdrawn because of its poor condition. It had become much darker, slightly softer, and tacky both inside and out.

TABLE II—PROPERTIES OF TUBING AFTER USE

Colour code	No. of transfusions	Reason for termination	Appearance after transfusion
Orange	45	Slight leakage in three places due to fine "pin-holes" in wall	Darker colour, still firm, little tackiness, slight softening
Black	34	Tacky inside and out	Tendency to break up inside
White	44	Slight leakage in two places due to fine "pin-holes" in wall	Darker colour, slight tackiness on inside and out, slightly softer
Red	33	Tacky inside and out; swelling on inside	Poor condition, beginning to disintegrate
Green	50	Slight leakage in two places due to fine "pin-holes" in wall	Slightly tacky, slight softening
Yellow	59	Slight leakage in two places due to fine "pin-holes" in wall	Very good condition, no tackiness, firm
Blue	31	Slight leakage in three places due to fine "pin-holes" in wall	Good condition, firm no tackiness

Some swelling had taken place on the inside surface, which was beginning to disintegrate.

Colour code green.—This was discontinued, after 50 transfusions, for the same reasons as "orange" and "white." Two fine "pin-holes" were found; otherwise the rubber was in good condition, although it had become somewhat soft and slightly tacky.

Colour code yellow.—This set was used for the largest number of transfusions, being withdrawn after 59. It had two fine "pin-holes" in the wall but was otherwise very good, showing no tackiness and remaining firm and superficially unchanged.

Colour code blue.—After 31 transfusions the set was withdrawn owing to the development of fine "pin-holes" in the wall. Apart from this the tubing was in a firm condition with no tackiness.

TABLE III—SUMMARY OF PATIENTS' REACTIONS

Colour code	No. of transfusions	Patients' reactions
Orange	45	One at 20th transfusion, severe rigor
Black	34	None
White	44	None
Red	33	One at 19th transfusion, severe rigor
Green	50	One at 6th transfusion, slight rigor
Yellow	59	None
Blue	31	None

These observations are summarised in table II.

Mechanical Properties Before and After Use

The yellow and orange tubings, examined for change in mechanical properties, gave the following results:

		Yellow	*Orange*
Unused tubing	Tensile strength (lb. per sq. in.)	600	840
	Ultimate elongation (%)	208	436
	Modulus at 50% (lb. per sq. in.)	85	—
After transfusions (Yellow 59, orange 45)	Tensile strength (lb. per sq. in.)	555	400
	Ultimate elongation (%)	260	336
	Modulus at 50% (lb. per sq. in.)	85	—
Percentage retention	Tensile strength	93	48
	Ultimate elongation	125	77
	Modulus at 50%	100	—

Patients' Reactions

Throughout the clinical trials a record was made of the number and severity of the reactions experienced by the patients undergoing transfusions from the various sets:

Colour code orange.—One reaction occurred at the 20th transfusion. This patient was very ill with anæmia due to carcinomatosis and had a severe rigor lasting ten minutes.

Colour code red.—One reaction at the 19th transfusion in a patient with myelosclerosis. There was a severe rigor, but the patient had influenza.

Colour code green.—One slight reaction at the 6th transfusion in a patient with severe lymphatic leukæmia.

There were no reactions with the other four types of tubing. The total number of transfusions was 296,

during which only 3 (1·01%) reactions were observed. These observations are summarised in table III.

Results and Observations

In 296 transfusions of whole blood, packed cells, or serum given through silicone-rubber tubing to patients attending the department of hæmatology, Manchester Royal Infirmary, during a period of seventeen months only 3 reactions (1·01%) occurred. This incidence of reactions is of the same order as has been observed with natural rubber tubing under similar conditions at the same hospital clinic (Stratton 1955).

The following advantages of silicone rubber were noted:

(1) The most satisfactory specimens of silicone rubber withstood a large number of sterilisations by autoclaving without serious deterioration in properties. Four different compositions of silicone rubber were in satisfactory condition for further use after over 40 transfusions, and one reached 59. In contrast, various natural rubber tubings under similar conditions showed much deterioration after 6–12 sterilisations.

(2) The general water-repellent properties of silicone polymers is well known (McGregor 1954). In the case of silicone-rubber tubing this leads to reduced wetting by fluids, including blood, and a reduction in the tendency to coagulate on the surface during a prolonged transfusion.

(3) The most satisfactory silicone rubbers used in this work, colour codes yellow, orange, and green, are transparent. This facilitates the important initial step of displacement of air from the tubes by saline solution.

(4) Silicone-rubber tubing is superior to natural rubber for procedures involved in separation, storage, and therapeutic use of blood-platelets, which adhere to natural rubber.

(5) Owing to its excellent ageing characteristics, silicone rubber can be stored for long periods without deterioration.

We conclude that, on the basis of their resistance to repeated autoclavings, their use for blood-transfusions, their transparency, and the ease of their fabrication, the silicone rubbers, consisting of a dimethylpolysiloxane gum, filled with either an amorphous precipitated silica or a pyrogenic silica (colour code orange and yellow respectively) are the most suitable of the tested rubbers for use in blood-transfusion.

Summary

The results of 296 transfusions of whole blood, packed cells, and serum through seven types of silicone-rubber tubing are reported. In the course of these transfusions only 3 reactions (1·01%) in patients were observed.

Because of its resistance to repeated sterilisation, its relatively long life in good condition, its transparency, and its physiological inertness, silicone rubber is superior in every way to natural rubber for blood-transfusion work and is recommended for this purpose.

The most satisfactory compositions of silicone rubber so far examined are a dimethylpolysiloxane gum filled with either an amorphous precipitated silica or a pyrogenic silica.

Our thanks are due to the medical, nursing, and technical staffs of the department of hæmatology, Manchester Royal Infirmary, for their help throughout these clinical trials.

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Symposia

BONE

IT is now an established custom in St. Andrews University that each year a prælector is appointed who is attached for a few weeks, usually in late August and September, to one or more of the departments of the medical faculty. This year Prof. P. Lacroix, of the Institute of Anatomy at Louvain University, holds the prælectorship, and during his visit he has been associated mainly with the department of physiology, Queen's College, Dundee, the orthopædic department at Dundee Royal Infirmary, and the anatomy department, St. Salvator's College, St. Andrews.

On Sept. 5 a symposium on bone was held in Queen's College, Dundee. The principal feature was a lecture by Professor Lacroix; but several members of St. Andrews University staff and Prof. G. M. Wyburn of Glasgow also contributed.

Prof. G. H. BELL referred to recent work by himself and Mrs. Oliver on experimental lathyrism in rats; in this condition the bone quality is reduced even when the inorganic component is not altered in quantity or quality.

Mr. J. A. GILLESPIE, in a communication on the influence of the nervous system on bone growth, stated that his experiments had led him to the conclusion that motor nerves have no direct influence on bone growth, but that they exert their effect indirectly through the action of muscles.

Dr. J. W. SMITH and Prof. R. WALMSLEY gave papers on experimental fatigue in bone, and correlated the variation in Young's modulus in different parts of the same bone with compression and tension forces and also with the orientation of the collagenous fibres in the osteons.

Professor WYBURN spoke on ectopic bone and stated that, although bone cells are not essential for the induction of osteogenesis in transplants, there is a more immediate response to fresh autogenous grafts, which suggests a more abundant or more active induction factor in fresh than in stored or prepared grafts.

Mr. J. HUTCHISON in a paper on dyschondroplasia and diaphyseal aclasis stated that he believed that in this condition there was a failure of ossification in the central parts of the epiphysis and also at its periphery.

Mr. I. M. STEWART gave an account of the preparation of cancellous bone homografts and said that there was no reported mention of this type of graft. He showed radiographs and photographs of a graft site at an explorative operation to prove the efficacy of the material.

Mr. I. S. SMILLIE, in a communication on osteochondritis dissecans, reviewed the subject of loose bodies in joints and expressed the view that they resulted from trauma. He pointed out that the classical loose body always contained bone, and that when this became detached a fracture might occur in the bone that immediately underlay the articular cartilage.

Professor LACROIX, speaking on bone growth and repair, began by reviewing the growth process in the region of the epiphyseal cartilage of a quickly growing bone, and referred especially to the complex structure that may be observed at the periphery of the epiphyseal cartilage. When epiphyseal or "growth" cartilage is transplanted to various sites it produces endochondral bone similarly to the process in situ. After a few weeks this transplanted cartilage has reconstituted at its peri-

phery the complex structure that is a feature of normal bone, and this is to be regarded as an induction phenomenon. Until a decade ago it was considered that such an induction phenomenon was linked with the presence of an organiser that differed from the inducing tissue, but numerous experiments cast doubt on this view. Professor Lacroix then described some recent experiments in which dead epiphyseal cartilage transplanted under the capsule of the kidney constantly resulted in the formation of bone in that site whereas ordinary hyaline cartilage, similarly transplanted, is non-osteogenic. This has led to the conclusion that induction processes are concerned in bone growth but that their exact nature is still obscure.

Before considering the process of bone repair, Professor Lacroix analysed his experimental results in grafting periosteum and bone-marrow. He found that periosteum from newborn animals produced cartilage in addition to bone; and even adult periosteum, although inactive before being grafted, constantly produced bone after transplantation. Bone-marrow has also been found to be osteogenic after transplantation, but the resulting bone tends to be absorbed. In long-term experiments the ossicle developing after transplantation of the cartilage from callus was found to have a histological appearance almost identical with that of diaphyseal bone. Professor Lacroix went on to say: "We deem therefore that the cartilage callus does more than merely weld provisionally the pieces of a broken bone; it not only provides the welding material but integrates this welding material into the organisation of the bone undergoing repair." Bone tissue is also constantly obtained when callus cartilage that has been killed by soaking in alcohol is transplanted, and it therefore appears that induction processes play a rôle in bone repair as they do in bone growth.

In conclusion Professor Lacroix correlated his experimental findings with the clinical picture of post-traumatic osteoporosis. Normal internal remodelling is most extensive in the region of the bone metaphysis, and it is in this very site that post-traumatic osteoporosis begins to be seen radiographically. Post-traumatic osteoporosis was shown to be associated with an internal remodelling of the bone that is more active than normal.

Medicine and the Law

A Murder Conviction Quashed

IN the Court of Criminal Appeal on Aug. 21, the conviction of an American airman for the murder of Walter Beaumont, aged 27, who had died at Hull Royal Infirmary on May 12, 1956, was quashed. Medical evidence called on behalf of the appellant in the Appeal Court suggested that the treatment given to Beaumont at Hull Royal Infirmary had been palpably wrong.[1]

Leeds Regional Hospital Board has now unanimously approved a report vindicating the staff of the Infirmary. The report, signed by three medical assessors (Prof. J. H. Biggart, Prof. John Bruce, and Dr. F. M. Parsons), follows an inquiry held on Sept. 5.

The assessors find that "Beaumont's treatment at Hull Infirmary was exemplary"; and they pay tribute to the care and devotion shown by Mr. M. A. Morkos, the surgical registrar, who moved into residence in the hospital and stayed there, scarcely leaving the patient's side, from the time his postoperative state took an obviously serious course. The assessors, in the light of their scrutiny of the post-mortem material and of the case-record, make the following observations:

"(1) There is histological evidence of severe damage to the kidney tubules (lower nephron nephrosis), which could only have originated soon after his injury, and was sufficient to have resulted in death.

"(2) The autopsy showed extensive pulmonary lesions. These were septic in type, and vascular and perivascular in situation, indicating that they had resulted from the transport of small infected clots. The lesions contained coccal organisms, and there is no evidence of the presence of fungi or yeasts such as are sometimes seen in patients treated with antibiotics.

"(3) Early meningitis was demonstrable at autopsy, and we regard this as further evidence of a blood-borne infection.

"(4) Death was hastened by the development of a catastrophic postoperative enteritis. We have carefully considered the relationship of this to the administration of terramycin. We are aware that this complication sometimes arises in patients treated with terramycin and other broad-spectrum antibiotics, but in these cases the cause of enteritis can be established as due to antibiotic-resistant staphylococci rather than to any inherently poisonous property of the drugs. In the present case, culture of the stools failed to yield staphylococci, and we must therefore regard the cause of the enteritis as an open question, since a similar and fulminating enteritis sometimes occurs after operations, especially on the abdomen, without any antibiotic therapy. In one view, the latter type of postoperative enteritis is the sequel to a period of low blood-pressure, and the occurrence of hypotensive lesions in the kidney lends support to such a possible explanation in this case.

"(5) The use of terramycin initially in Beaumont's case was in our opinion not incorrect, and there is good evidence of its value in the treatment of peritonitis. Its withdrawal at the onset of diarrhœa was correct. By this time, the patient had developed a fulminating gastro-enteritis as well as chest lesions, and these did not respond to penicillin. It was possibly unwise of the resident surgical officer to resort again to terramycin; but since there was reasonable doubt about the cause of the enteritis, and since the patient was gravely ill and febrile despite the administration of penicillin, the renewal of terramycin therapy was not unreasonable and certainly not blameworthy. In any event, the small quantity of terramycin which was then administered had no influence of any kind on the outcome of the case. We believe, in fact, that before the second course was started, the patient's state was irreversible.

"(6) It seems to us that the management of the fluid-electrolyte state should be considered in relation to three periods of the man's illness:

(*a*) *In the preoperative and operative period*, the management of the fluid-electrolyte situation in our opinion was adequate.

(*b*) *In the early postoperative phase*, the control of the fluid therapy was appropriate.

(*c*) *In the late postoperative period*, following the development of severe enteritis complicated by serious renal impairment and by lung infection, a highly complicated biochemical disturbance developed. The fluid loss from the bowel was enormous and resulted in profound dehydration, one evidence of which, apart from the careful clinical observations of Mr. Morkos, was the concentration of hæmoglobin in the blood (114%). As soon as possible, Mr. Morkos enlisted the aid of the hospital biochemist who thereafter performed daily estimations on which the day-to-day administration of fluids was based. The amount of fluid administered may appear large to those unfamiliar with the management of severe gastro-enteritis or cholera which this man's diarrhœa resembled. It was perhaps fortunate that Mr. Morkos had had some experience of the treatment of cholera, and had the courage to apply this experience in the management of this extremely difficult case. That the amount of fluid given was in no way excessive is borne out by the absence at autopsy of the usual findings of overhydration, as, for example, œdema of the lungs, fluid in the serous cavities, or generalised dropsy."

"It is our impression," the assessors add, "that Beaumont was on the point of death on the fifth postoperative day"; and his survival for a further three days was due, in their opinion, to energetic and competent measures. "In the event, and in the light of all the evidence, however, this man's life was unsaveable and his death was not in any way attributable to the treatment he received in hospital."

1. See *Lancet*, Sept. 1, 1956, p. 459.

In England Now

A Running Commentary by Peripatetic Correspondents

THERE is an air of embarrassment in the unit just now. Our registrar, the clever one, instead of bombarding the chief with unheard-of syndromes named after unpronounceable Slavs, is holding his place meekly at second from the end in the ward-round queue. I am sure the chief thinks he has gone on holiday.

The trouble started when one of that fast-fading clan—the gentlemen of the road—was admitted on the verge of diabetic coma. A known diabetic he carried a grubby card which gave his insulin requirements and a few other particulars. In a paper-wrapped bundle, along with some other oddments, lay his syringe and needles. He admitted that he had been a bit irregular with his injections of late but as it hadn't interfered with his appetite he hadn't bothered. He obviously had not washed for weeks.

Our registrar asked him what methods of insulin administration were employed by those for whom a regular toilet was an unpleasant thought rather than a happy action. Our patient laughed at the thought of cleansing his skin before giving himself a "sticker." He injected himself through his trouser leg like everybody else did, he supposed. It was dead easy and it hadn't done him any harm yet. Sure enough, the thighs, while dirt-encrusted, were free from the scars of any previous misadventures.

Pale with horror, our registrar, like a missionary in an alien clime, lectured him on the error of such ways. He pointed out the dangers, the complications, the ills, and the miseries that ignorance would bring. With his own hands, he decided, he would demonstrate how an injection should be given. After several minutes of hard work the skin was clean. The syringe carefully sterilised, the correct amount of insulin was measured, and the area injected in the approved painless way.

The tramp, despite the registrar's careful commentary, was, on the whole, not impressed. He was even less impressed two days later, when the abscess began to form.

* * *

Many doctors take an interest in music, but it is seldom an active help in general practice. The exception occurred during the annual general meeting of our local choral society when a bus demolished a car outside my house. Suspending the chairman's speech for a short while, the social committee quickly added the incident to the agenda of the meeting. Some members helped the injured into my consulting-room, while two sopranos mopped up the blood, the altos fetched relays of hot water, and the conductor telephoned for an ambulance. One burly tenor did yeoman work by sitting on a young lady in hysterics, while I had a surgical duet with an ex-nurse soloist stitching up cuts and stopping arterial bleeding. As we patched up the injured, two basses helped to carry them out to the waiting ambulance. The local reporter who was attending the meeting took particulars of the accident, and the honorary secretary, a professional photographer, took flashlight pictures of the smash for the local paper and the police. Between them, they even provided all the details for the R.T.A. claim. Within minutes of the last casualty being carried out, the normal agenda was resumed, the meeting concluded, and a small group of enthusiasts stayed on to practice an unaccompanied 17th century polyphonic mass as if nothing had disturbed the peace. Who said musicians were temperamental?

* * *

Miss Jenkins's greatest mistake, I suppose, was to take her baby to the hospital. I could easily have dealt with the situation—that irritating triviality of an infant's nether region for which pædiatricians seem unable to find a scientific name. But this time it had to be the hospital.

The earnest young doctor at the hospital carefully avoided the morals of the case, but, finding that the baby had a small head and a systolic murmur, immediately accused Maisie of having had german measles six months previously, which she stoutly denied. A conference with the registrar, assistant, and chief followed, and one by one they all had a go, but she remained adamant. The almoner was summoned to tempt her with home-helps, meals-on-wheels, and all the panacea of the welfare State, if only she would change her mind. When the gentle methods of the almoner had failed, sterner measures were applied. Maisie was kept waiting about in the outpatient department, which was not very difficult to arrange, and was interrogated by a different doctor each time, which was even less difficult. Sometimes a succession of students was sent to torment her, all with the same question. She was assigned to one of the ward-sisters, who had a well-earned reputation for the difficult case, but still her story remained unshaken.

A series of clinical conferences was given in her presence when the chief made a great point of demonstrating the baby as an example of the rubella syndrome. Everybody referred to it knowledgeably as "that R.S.," and the registrar wrote in his summary " . . . undoubtedly a classical case, although the mother has not admitted it yet." Maisie was weakening physically but stuck to her guns, and her resistance became acutely embarrassing to the hospital authorities. Every now and then a tactless student would ask why she had not had rubella; her notes could not be accurately coded and were always getting lost; no treatment could be started until the other business had been cleared up. It grew out of all proportion and became one of the most pressing research projects. A succession of young doctors tried their hand, but matters came to a head when one of them decided to write an article. A confession, a written one at that, was now imperative. No-one will ever know how he managed it. But after nearly two hours, he emerged from behind closed doors, clutching a piece of paper which bore the cryptic message:

"I now admit I had German measles while I was carrying."
Signed MAISIE JENKINS.

The other day I came across an article describing some allegedly rare combination of troubles after maternal rubella. It's a pity he went to all that trouble, because I could have told him that Maisie had had two others just like it. I could have told him about the village odd-job man—he's got a small head too. But then, I wasn't asked.

* * *

In poliomyelitis the Scientists and Preventive Medicine Men are already showing us the way to go. In a few years, it seems, they will be showing one more group of clinicians the way out. We are used to it, of course. Fevers have shrunk to the accommodation of waifs with dysentery; pædiatrics has become a matter of tantrums, encopresis, and strange biochemical babies; children's orthopædics has sunk to the contemplation of flat and funny feet. And so, surveying with some disdain the confusion appearing among our colleagues in "chests," we prepare to shorten our lines and abandon another province of a once mighty empire to the ever advancing geriatric hordes.

But perhaps for us clinicians who deal with poliomyelitis, there is still hope. We know something of respiration and breathing-machines. We understand a little of muscles acting without gravity. Our days and nights have been made hideous by the very hums, squeaks, and hisses used by Charles Chilton for his effects. Perhaps from those among us who can match that monumental integrity portrayed by Guy Kingsley-Pointer may be chosen the Docs to make the Journey into Space.

* * *

She was 78 and more than a little confused. It was difficult to picture her youthful, agile, riding a "rosin-back" and going through what she described as "hoops and all that."

As she was leaving the clinic she suddenly turned. "Are you from Sanger's," she asked, "or Bertram Mills'?" Sister was delighted; not every patient recognises me as a trick-cyclist.

* * *

Seven white coats working in a lab.,
One off on holiday—one taken bad.
Five white coats working in a lab.,
One gets pyrexia-U.O.—how sad!
Four white coats working in a lab.,
One gets tummy pains—poor absent lad.
Three white coats working in a lab.,
If another goes sick—two go mad!

Letters to the Editor

THE FINAL EXAMINATION

SIR,—May I respectfully suggest that Sir John Conybeare (Sept. 8) and Dr. Douglas Hubble (Sept. 15) have not heeded the examiners' customary injunction to read the question carefully before attempting an answer. In the example of the multiple-choice question quoted by Professor Bull the candidate was not asked to make a diagnosis, but to state what he would do when faced with a certain situation. Surely answer no. 2 is the correct procedure.

It is certainly comforting to patient and doctor if diagnosis can precede treatment, and it is true that in real life there would probably have been further information to be derived from the circumstances and examination, which would have enabled the doctor to make a more certain differentiation between diabetic coma, hypoglycæmic coma, and the many other possible causes of unconsciousness in a diabetic patient. Nevertheless I would submit that in practice it is not always easy to make a bedside diagnosis of the cause of coma in a diabetic. Perhaps the examination question has been deliberately worded to leave the candidate in doubt.

Now, if the patient's coma is due to hypoglycæmia, procedure 1 (injection of insulin) will almost certainly kill him; procedures 3 and 4 (delaying tactics) may well do so, whereas procedure 2 (intravenous injection of glucose solution) will usually produce a quick recovery. If, on the other hand, he is suffering from diabetic coma or cerebral hæmorrhage, injection of glucose will do no harm and one common condition will have been eliminated from the differential diagnosis.

There are relatively few circumstances—and the above is an example—in which a correct and prompt decision by a doctor will make the difference between life and death, and probably more situations in which an incorrect and prompt decision will have an equally dramatic but less fortunate effect.

Whatever else a medical student should know by the time he qualifies he should at least be familiar with these situations. It should be possible for panels of physicians, surgeons, obstetricians, &c., to prepare lists of these situations and to agree on the procedures to be adopted. A list of, say, fifty questions and answers should be made available to every student preparing for his final examination. It would then be obligatory for him to give the "approved" answer (even if he did not approve of it himself) to each of the fifty questions to, say, the door-porter at Examination Hall before proceeding upstairs to start the traditional examination. This simple procedure would at least prevent the young casualty doctor from going off to find his textbook when a patient collapses after an injection of antitetanic serum, because he has happened to miss the appropriate lecture in his student career, or prevent the young doctor on seaside holiday from leaving the application of artificial respiration to the nearest boy scout.

Institute of Child Health,
Hammersmith Hospital, London, W.12. J. P. M. TIZARD.

SIR,—Sir John Conybeare and Dr. Douglas Hubble, the big guns, have fired. No longer am I afraid to admit that I too could not solve Professor Bull's coma conundrum.

One of the functions of statistical analysis is to give practical men elegant reasons for believing what they already know. On this score I have nothing but praise for Professor Bull's erudite article. Another function of statistical analysis, the importance of which William Sealy Gosset, the great "Student," never failed to emphasise, is to form a basis for practical decisions. On this score, without wishing in any way to belittle Professor Bull's valuable article, I can give him few marks. The recommendation "that more use should be made of the multiple-choice technique of examining, which eliminates marking error" has no basis in the statistical analysis. It certainly eliminates marking error; but it does not eliminate examiner error, as evidenced by the fact that two such eminent clinicians as Sir John Conybeare and Dr. Hubble did not know for certain the appropriate answer; and it introduces a more serious error—chance. By using the plumping method of Dr. Hubble candidates would on average get 25% of the marks, and without any knowledge of medicine whatever their marks might range from none to a hundred. If such a recommendation is acted on, the final examinations of our medical schools will be reduced to the level of football pools.

Professor Bull's article serves a most useful purpose. It calls attention to errors in examination, which everyone must deplore; and experiments should be planned on which practical recommendations can be based. This can be done if "Student's" dictum is observed. "The art of designing all experiments lies even more in arranging matters so that r_{AB} is as large as possible, than in reducing σ_A^2 and σ_B^2." [1]

The deplorable practice of modern examiners of only using a small range of marks—say 45% to 65%—is dismissed by Professor Bull as an unimportant source of error. Certainly it is unimportant in so far as it reduces the standard deviation of an examiner's array of marks; but it is an important source of error in that there are strong reasons for believing that it reduces the coefficient of correlation between the marks given and the ability of the candidates. In the extreme case the examiner is shirking his responsibility of marking the papers and replacing marks with the superficial personal judgment—pass, doubtful, or fail.

Every practical examiner and every practical student knows that there are good, bad, and indifferent candidates. Good candidates probably pass, bad candidates probably fail, and indifferent candidates are probably given the benefit of the doubt—quite a good state of affairs really. There are also good, bad, and indifferent examiners—not such a good state of affairs. The bad examiners should be eliminated by examination.

Finally I make a practical suggestion. A board of students should be set up for examining examiners in the art of examining. Such questions as, "What range of marks would you use in marking a paper? Give reasons for your choice" might be asked. In this way the fees would circulate and a smaller proportion fall into college chests—in itself not a bad thing.

London, W.1. GEOFFREY E. LOXTON.

A MURDER CONVICTION QUASHED

SIR,—In his letter last week Dr. Stott asks: "would it not be wise for general practitioners who have previously attended a person who dies suddenly to be summoned to give evidence at the inquest?" I would say most wise. In fact it should be the universal practice and should include senior hospital clinicians where hospital cases are involved. Most pathologists who conduct medicolegal post-mortem examinations would welcome this clinical opinion in court, for then clinical opinion would be expressed by those best qualified to give it and the pathologist would not be put in the position of having to appear to be expert in fields other than his own.

Chapel Brampton,
Northants. R. M. HEGGIE.

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SOME EFFECTS OF B.Z. 55 ON THE CARBOHYDRATE METABOLISM OF DIABETIC PATIENTS

SIR,—The antidiabetic action of certain sulphonamides has been the subject of much recent work, some of which was reviewed in your leading article of July 28. Inhibition or destruction of glucagon-secreting α-cells, insulin-sparing action, insulinase inhibition, increase of insulin production, and depression of gluconeogenesis have been proposed as possible explanations.

Twelve diabetics, who did not require insulin treatment, were given oral sulphonamide (B.Z. 55), and intravenous glucose-tolerance tests, intravenous insulin tests, and combined intravenous glucose and insulin tests were then performed.

It has been shown previously that from the data of the glucose-tolerance test one can calculate a factor which indicates the rate of glucose uptake by the tissues —the glucose-assimilation coefficient.[1-3] This factor is related to the presence of active insulin in the tissues [4]: its value in normal individuals is $1{\cdot}8 \pm 0{\cdot}3$, in diabetics $0{\cdot}5 \pm 0{\cdot}2$.[2] Mathematical analysis of the hypoglycæmia induced by intravenous insulin yields two factors—one corresponding to the actual hypoglycæmic effect of the hormone (factor i), the other (factor a) expressing the glucose output by the liver.[5]

The combined glucose-insulin injection is also followed by a glucose regression curve, analysis of which expresses the activity of the injected insulin.[3]

All our patients showed the same reduction of blood-glucose and glycosuria as has been described by several authors. In only four of the twelve, however, was there any improvement of the glucose-assimilation coefficient. Such improvement, which might indicate an increase in the quantity or activity of endogenous insulin, was not only inconstant but, when present, was transient—though the improvement in the level of glycæmia and glycosuria persisted during several weeks' treatment. In all but one patient the glucose-assimilation coefficient returned to pre-treatment level (mean value before treatment, $0{\cdot}77 \pm 0{\cdot}3$; after one week of treatment, $1{\cdot}02 \pm 0{\cdot}6$; after several weeks, 0·86). The individual and transient changes are probably due to a stimulating action of the sulphonamide on surviving β-cells. Such an action has been demonstrated in normal rats.[6]

There was no consistent change in the action of exogenous insulin as judged by the combined glucose-insulin tests or by the values of the factor i calculated from the intravenous-insulin tests. This observation seems to rule out a true insulin-sparing action of the sulphonamide.

The only definite change observed in all the patients was the very marked depression (in most cases the disappearance) of the output of glucose by the liver during the insulin-induced hypoglycæmia. The factor a, which expresses this glucose output, was 1·5 before the treatment, 0·3 after one week of treatment, and 0·1 after thirty to sixty days. ('Student' test with pairing $t = 6$; $n = 10$; $p < 0{\cdot}001$.) This observation is in keeping with recent reports suggesting that the sulphonamides producing hypoglycæmia inhibit important enzyme systems (among them glucose-6-phosphatase) in the liver.[7] The reduction of glucose output by the liver and the re-utilisation of glucose might explain why the blood of diabetics treated with B.Z. 55 or related compounds contains an excess of pyruvate [8] and also explains the lowering of blood-glucose and the increase in body-weight.

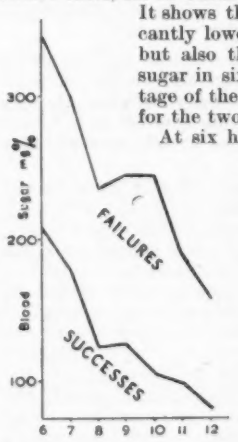
Clinique Médicale,
Hôpital Universitaire Saint-Pierre,
Brussels. PAUL BASTENIE.

RESPONSIVENESS TO ORAL HYPOGLYCÆMIC AGENT

SIR,—We have noted with interest the letter from Dr. Ghanem and Dr. Mikhail (Sept. 8). The problem of devising a method to anticipate any particular diabetic patient's response to an oral hypoglycæmic agent has occupied our attention for some time.[9]

For the first five days after admission our patients were maintained without insulin on diet alone. Once this initial control period was completed a two-day test was performed. On these two days no breakfast was given, but on the second day B.Z. 55, in a dose of 50 mg. per kg. of body-weight, was administered by mouth. This sequence enabled us to assess the effect simply of omission of breakfast. In a first group of twelve patients, blood and urine levels of sugar and sulphonamides were examined hourly for six hours, while in the subsequent thirty-three patients test samples were obtained every three hours under the same conditions. The patients were kept in hospital and maintained on B.Z. 55 for at least a further five days; observation was then continued in the outpatient department at least twice weekly. Cases were divided into successes and failures according to whether successful maintenance therapy with tablets alone could be obtained.

The accompanying figure shows the results in the first twelve cases, six of which were successes and six failures.



It shows that the successes have a significantly lower mean blood-sugar at 6 A.M., but also that the over-all fall of blood-sugar in six hours estimated as a percentage of the initial value is about the same for the two groups.

At six hours the group of failures still have a high blood-sugar, owing to the high initial value. The figure incidentally also shows that in the failures, and to a lesser extent in the successes, the fall of blood-sugar appears arrested temporarily between 8 and 10 A.M., and some counter-mechanism could be suspected, which may show its full effect only on the chronic maintenance dose. Our remaining patients show results which fit in with this report.

It therefore appears to us, contrary to Dr. Ghanem and Dr. Mikhail, that the acute test, though of interest to the series as a whole, offers no help in anticipating the reaction of the individual case to the drug. The fasting blood-sugar level was in none of our successful cases more than 275 mg. per 100 ml. In our failures the fasting blood-sugar level ranged from 123 to 421 mg. per 100 ml.; and, though in many there was a significant drop at the initial test dose, subsequent maintenance therapy failed to prevent hyperglycæmia and glycosuria. A further more detailed account of this aspect of our work is in preparation, but we consider it proper to stress these findings once again to prevent maintenance therapy being considered as a result of an acute test alone.

Whittington Hospital, London, and Biological Control Laboratories, Wellcome Foundation, London. FREDERICK W. WOLFF
G. A. STEWART.

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THROMBOSIS OF THE SIGMOID SINUS

SIR,—I have been very interested to read the experiences of Mr. Reading and Mr. Schurr (Sept. 8) and the letter which has followed from Mr. Maxwell Ellis.

Memories from earlier years of cases of otitic invasion of the lateral sinus arouse in me the old feelings of anxiety—an anxiety which in due time was eased when I learned from the writings of S. H. Mygind that at Kommunehospitalet in Copenhagen it was his practice, following that of the late Dr. Holger Mygind, not to open the sinus after dealing with the primary focus in the mastoid unless the vessel was thought to contain pus; nor was it usual to tie the internal jugular vein. Mygind thought that his results were as favourable as those of some others who treated the venous system more radically.

I am happily reminded, and with gratitude to Mygind, of a case under the care of my colleague, Mr. John Roberts, where we followed Mygind's teaching at the first operation and then, after a reasonable interval of observation, performed a second to find, as expected, pus in the sinus, which was successfully drained. Here was a very good example of "laudable pus," but how different from those cases of aural bacteræmia with a fluid sigmoid sinus and vascular lung symptoms, which today we should expect to treat brilliantly with the new chemicals and antibiotics.

Liverpool. H. V. FORSTER.

UREA METABOLISM IN PROTEIN DEFICIENCY

SIR,—The method of determining the volume of water in the bodies of living persons by giving a known amount of urea by mouth, and then measuring the rise in the concentration of urea in the serum and the excretion of urea in the urine, has the merit of simplicity, and it requires no special apparatus or techniques. It has been found to give satisfactory results for normal and obese adults [1–3] and for moderately undernourished men.[4] Holmes et al.[3] have recently found, however, that the method gives results which seem extraordinarily high for the total body-water of malnourished, œdematous African men who have lived on a low-protein diet all their lives—87% of the body of one man was estimated to consist of water. These findings are similar to those of Gopalan et al.,[5] who applied the same method to grossly undernourished and œdematous men in India and found up to 90% of water in their bodies. Both groups of workers have suggested that the only way of explaining these results is to suppose that the cells of protein-deficient persons are very "dilute" so that their bodies contain an excess of intracellular as well as of extracellular fluid. This suggestion seems to be borne out by the observation of Holmes et al.[6] that if such persons are given a diet containing more protein than that to which they are accustomed they retain far more nitrogen than would be expected from their observed gain in weight. Nevertheless the values found for total body-water by means of urea still seem to be impossibly high. Any adult human body, however undernourished, has a skeleton, and the bone minerals in this skeleton must contribute at least 5% of the body-weight. If the body contains 90% of water and 5% of minerals, and even if it has no fat at all, there is only 5% left for all the protein in the whole body. A fœtus weighing 7 grammes contains a greater proportion of protein than this.

An alternative, or perhaps additional, explanation of the high values found for the total body-water of protein-deficient persons when urea is used as the test substance is suggested by some recent work of Holt and Snyderman.[7] These workers fed babies on diets containing decreasing amounts of good-quality protein, the calories being maintained with fat and carbohydrate. Eventually a level of protein was reached which was insufficient to enable the infants to gain weight. If nitrogen was then added to the diet in the form of urea the babies started to gain weight again, which Holt and Snyderman interpret as indicating that urea can provide "unessential" nitrogen for human growth. If in times of shortage urea nitrogen can be used for tissue growth in infants, why not for making good a protein deficiency in adults? This would explain the disappearance of some of the urea administered for the determination of body-water and the resulting high values for the volume of water that have been obtained. It might also be one reason for the low values found for the concentration of urea in the serum of children with kwashiorkor,[8] and the rise which follows treatment with a high-protein diet. The suggestion could easily be put to the test by comparing the values obtained for total body-water in protein-deficient persons by means of urea with those obtained by the use of some other substance such as antipyrine, deuterium oxide, or tritium. It could also be tested by giving urea to people who were deficient in protein and subsisting on very low protein diets, and following their retention of nitrogen by means of balance experiments.

If this suggestion is correct urea should not be used for determining total body-water in protein-deficient persons, and perhaps not even in healthy children; but "it is an ill wind turns none to good," and the possibility that the human body can use its own waste material for protein synthesis is of much greater fundamental importance.

Medical Research Council Department of Experimental Medicine, University of Cambridge. E. M. WIDDOWSON.

BENIGN ENCEPHALOMYELITIS

SIR,—We read with interest Dr. Jelinek's paper (Sept. 8) on two further cases of benign encephalomyelitis. Because of the epidemiological interest of such cases, we should like to add one of our own.

The patient, a woman aged 27 of Italian extraction, lived in East Ham and worked as a waitress. She was admitted to the hospital on May 10, 1956, with a two-week history of very severe lumbar pain, headache, and slight fever. At the onset there were no abnormal neurological signs, but soon the temperature rose more sharply, with neck stiffness, tenderness in all limb muscles, very brisk deep tendon reflexes, right ankle clonus, and bilateral extensor plantar responses. The blood-count was normal, the erythrocyte-sedimentation rate (E.S.R.) was 60 mm. in the first hour (Westergren), and the cerebrospinal fluid was completely normal.

This acute episode subsided within a week, but for the following two months low-grade fever persisted, with raised E.S.R. and variable intensity in signs of pyramidal-tract involvement. During all this time there was severe emotional lability.

Dr. Helen Dimsdale saw the patient in consultation and agreed that this was a case of mild encephalomyelitis, probably not of the "Royal Free type" as there was no enlargement of the lymph-glands. Electromyography (Dr. A. T. Richardson) showed some grouping of motor-unit potentials on minimal volition, suggestive of encephalomyelitis of the Royal Free type.

Other investigations, including Paul-Bunnell reaction, Wassermann reaction, blood-cultures, and complement-fixation test for toxoplasmosis (Dr. I. A. B. Cathie) were negative; but electrophoresis of the serum-proteins showed inversion of the albumin-globulin ratio, with marked increase in γ-globulin.

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The patient was discharged from hospital on June 19, improved, without frankly abnormal neurological signs, and with an E.S.R. of 20 mm. in the first hour.

She has gone to Italy for convalescence, and we understand from her relations that she has not so far relapsed.

The Italian Hospital, London, W.C.1. V. BONOMINI E. MONTUSCHI.

PARAPLEGIA FOLLOWING SPINAL ANÆSTHESIA

SIR,—I agree with your correspondents who regard spinal anæsthesia as an outmoded method which should be abandoned. I do not believe that its harmful consequences can be attributed to contamination of the anæsthetic solution by phenol; for in Finland the ampoules are never stored in phenol solution yet I have seen 6 patients with paraplegia following spinal anæsthesia. Those who practise the method seem to become blind to its disadvantages: for instance, severe (and often persistent) headache is regarded as "normal," like vomiting after ether narcosis; and I remember a case in which the paraplegia was at first attributed to hysteria.

The discussion, I suggest, could easily be terminated by the following scheme. On a certain day at a certain hospital the surgeons who favour spinal anæsthesia will meet the surgeons who favour narcosis; and then all those who claim that spinal anæsthesia is free from risk will undergo spinal anæsthesia, while the others have half an hour of ether narcosis. I do not think there will be many supporters of spinal anæsthesia at that meeting; and the reason is that spinal anæsthesia is dangerous—indeed highly dangerous in unskilled hands.

Finland. CLAES CEDERCREUTZ.

*** In view of some possible fallacies in the result of this experiment, we suggest that it should be conducted under the auspices of the Medical Research Council.—ED. L.

ROSEOLA INFANTUM

SIR,—In your columns recently Letchner [1] has reviewed 50 cases of roseola infantum, Fletcher [2] and Reis [3] have recorded other outbreaks, and additional information has been given by Keizer [4] and Leffkowitz.[5] I should like to make some further remarks on this striking but seldom-reported infectious disease, of which we have seen about 100 cases in two years at this Warsaw clinic, directed by Prof. J. Bogdanowicz.

Sometimes there is an acute stage with high fever, which may lead to energetic but ineffective antibiotic therapy. The disease is more likely to be recognised if the physician bears its existence in mind and remembers that 70% of the cases occur between the 10th and 18th month of life. At first there will be no focal signs, but a white-cell count on the second or third day of the illness will give the clue. Examination of the blood has enabled us, in some cases, to make a definite diagnosis before the temperature fell and the rash appeared.

Roseola infantum is seen particularly in children who have been carefully guarded from infection by keeping them away from children's centres. It is usually their first feverish illness and it attacks all the children in a family successively, during their 2nd year of life. This suggests that the adults may be carriers—possibly with virus in their stools, as in poliomyelitis. Certainly, contact with a sick child is not necessary for infection: thus we have lately seen a typical case in a baby aged 13 months, who had been for six weeks in a surgical department for adults.

Three years ago, when we acquainted our colleagues, working in this clinic, with the characteristic manifestations of roseola infantum, it turned out that most of their own children born between 1953 and 1956 had had the disease. It looks as though roseola infantum were in fact one of the commonest febrile diseases of infancy.

I append an account of 2 cases with exceptionally violent and alarming signs, rarely reported.

CASE 1.—A boy aged 9 months—an only child and normally developed—had been very carefully isolated from other children, and had never been ill before. The onset was sudden, with high temperature, vomiting, and abdominal pain. His general condition was bad; he was sleepy and apathetic, and woke with a cry. Temperature 40°C. Clinical examination did not reveal any cause for the illness: nothing abnormal was found in the nasopharynx, abdomen, or the muscular and nervous systems. On the second day the child's condition was much worse, with loss of appetite, vomiting of blood, and blood in the stools several times during the day. Temperature 40°C. Further examination revealed no abnormality, and after observation in their clinic, the surgeons found no sufficient reason for laparotomy. A white-cell count showed leucopenia (4200 leucocytes per c.mm.) with lymphocytes 75%. On the fourth day of the illness the temperature came down, and a few hours later the characteristic rash appeared on the trunk and face.

CASE 2.—In a girl aged 4 years the onset was sudden with a temperature of 40°C, abdominal pain, and meningo-cerebral symptoms. On clinical examination no cause could be found for this, and the cerebrospinal fluid was normal. In the blood the white cells numbered 4200 per c.mm. with 72% of lymphocytes; and we diagnosed roseola infantum. The temperature was 39–40°C for three days, but on the fourth day it came down to normal, and after a few hours a rash of large discrete pink spots appeared on the trunk.

Clinic for Infectious Diseases of Infancy, 37, Wolska Street, Warsaw, Poland. H. SZCZEPAŃSKA Lecturer.

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2. Fletcher, F. R. *Ibid*, 1956, i, 50, 347.
3. Reis, N. D. *Ibid*, p. 830.
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INSULIN AND CHLORPROMAZINE IN SCHIZOPHRENIA

SIR,—Dr. Boardman and his colleagues (Sept. 8) make the statement, admittedly qualified, that "there is, therefore, some evidence that chlorpromazine is a more effective method of treating schizophrenia than is insulin." Though this may be possible, it would seem that there is no justification for drawing this conclusion from the data which they submit.

In the first place, it is wholly misleading to make such statements as "Chlorpromazine appears to be a more effective form of treatment [than insulin] . . . but the difference is slight and is not statistically significant." Since the data has been submitted to the χ^2 test, results must be interpreted in the light of that test, which only measures whether observed differences are in fact likely or unlikely to be the result of chance. In fact, *no* significant difference was found between results of treatment with insulin or chlorpromazine.

Secondly, the only significant difference recorded was in the length of stay in hospital, which was shorter in patients treated with chlorpromazine. The authors use this as additional argument in favour of chlorpromazine, where they state that "the difference cannot be disregarded." Closer inspection of this part of the data suggests, however, that it certainly *should* be disregarded. Not only are no criteria given for discharge but also it appears that some patients in both groups were subjected to other forms of treatment prior to discharge. This is mixing matters with a vengeance.

Thirdly, we are told that environmental influences were kept as strictly equal as possible. It would be possible to argue, therefore, that, as there was no significant difference in results with either method of treatment, any improvement was due to the beneficial influence of the common environment.

Finally, the suggestion that chlorpromazine is more effective than insulin, no matter what reservations are added, cannot be substantiated without an adequate follow-up. The authors quote several studies to illustrate the disagreement between investigators on the value of insulin. These studies, however (and there are many more), are almost unanimous on the improvement immediately following treatment. Such results are notoriously

misleading. It is the relapse-rate which should qualify the statement that "Chlorpromazine is the first treatment of choice in schizophrenia."

Netherne Hospital,
Coulsdon, Surrey. A. R. MAY.

DEAF OR BACKWARD ?

SIR,—Your annotation last week is timely in that it draws attention to the need for careful differentiation between deafness, mental defect, and their combination. But your conclusion that where behaviour problems occur "there is yet no means of making a satisfactory diagnosis" seems unnecessarily gloomy.

Before the age at which deafness and consequent frustration result in neurotic reactions, mental deficiency may be detectable in delay in motor development (including delay in reaching the traditional milestones); in the case of the older child a history of such delay is a valuable pointer.

Again, the development of voluntary activity is accompanied in its early stages by modification of infantile reflex behaviour, and, in the young child, progress of this modification may be taken as evidence of progress of volition—of mental development.[1] That this is possible even where neuromotor defect coexists has been confirmed in a study of neurally abnormal babies carried out by Eirene Collis and myself in the welfare clinics of the London County Council. The method is especially valuable since it may enable the differentiation "deaf or backward" to be made before neurotic reactions to deafness develop and at that early age at which speech training can best be begun.

London, W.1. WILLIAM DUNHAM.

INTESTINAL OBSTRUCTION DUE TO FOOD

SIR,—Mr. Rains and his colleagues suggest (Sept. 1) that cellulose, methylcellulose, or carboxymethyl cellulose might cause intestinal obstruction.

These substances have different physical and chemical properties and, as far as I am aware, no cases of obstruction have ever occurred following ingestion of pure methylcellulose.

In colostomy and ileostomy cases, methylcellulose gives a patient control, and its property of absorbing fæcal odours is virtually unique in a palatable non-toxic substance. The patients are saved unnecessary embarrassment and can continue in their chosen occupation without being a nuisance to fellow employees. This is of particular interest to practitioners—especially industrial medical officers—who are often asked to intercede, especially during hot weather.

Derby. O. P. LLEWELLYN.

SIR,—The reference by Mr. Rains and his colleagues to the use of cellulose products in medicine and foods prompts me to clarify the differences between methylcellulose and carboxymethylcellulose.

Methylcellulose is a pure synthetic product, manufactured under conditions which ensure uniformity in chemical composition and in physical properties. In solution, methylcellulose is a hydrophylic colloid which is not ionised. The viscosity is unaffected by pH changes over a range of 2–12, it swells to a soft gel in the stomach acids, the viscosity of the gel is unaffected by the alkaline conditions in the duodenum.

A methylcellulose gel is characterised by clarity, uniformity, and softness. Solutions have a lower surface-tension than water, and its protective colloid powers are valuable in reducing any irritation caused by roughage in the diet.

Machle et al.[2] showed that, on feeding methylcellulose to humans, the product passed through the digestive tract unchanged, and feeding trials on rats produced no significant changes in the growth picture.

Monaco and Dehner [3] have demonstrated that dispersions of methylcellulose of relatively low viscosity have a greater water-retentive capacity than equally concentrated natural gum dispersions of greater viscosity, and this is clinically significant in cases of diarrhœa, ulcerative colitis, and colostomy.

Carboxymethylcellulose is commercially the sodium salt (S.C.M.C.). This is ionised in aqueous solution, and in the presence of stomach acids is decomposed into free carboxymethylcellulose, which sometimes separates as a glutinous, putty-like mass which persists even after treatment with intestinal juices. Moreover, S.C.M.C. is unstable in the presence of alkaline earths and heavy metals, and insoluble salts are produced by hard water—a significant fact when it is remembered that a copious drink has to be taken with the dose when this type of product is used as a bulk laxative or as an appetite suppressor.

'Celevac,' which is methylcellulose in an acceptable form, has never caused intestinal obstruction, whether it is used for chronic constipation, necessitating a long drink with the dose, or for controlling a colostomy, correcting diarrhœa, or as an adjunct in the treatment of ulcerative colitis, when the dose is taken with a minimum of liquid.

Harker Stagg Ltd.,
London, E.1. R. L. SWAN.

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PRIMARY ALDOSTERONISM

SIR,—Professor van Buchem and his co-workers, answering last week some of my remarks on their recent paper, make some interesting points—for example, concerning the effect of aldosterone and potassium on carbohydrate metabolism. They also point out that growth can be retarded by potassium deficiency, which, they say, may be related to the fact that potassium is needed for the formation of cytoplasm; thus, they imply that one should not seek an endocrine anomaly to explain the stunted growth and hypogonadism of the case they described (Aug. 18).

I do not want to go into a detailed analysis of the statements and references cited about the effect of potassium on growth. Suffice it to say that Brokaw, for example, based his work on very young rats and noticed that an initial drop in growth tends to diminish with time.[1] Also, if the effect of potassium on growth is related to the formation of cytoplasm, one might expect a degree of cachexia which would then explain, too, the delay in the onset of puberty in Selye's terms [2]; yet such cachexia, or even signs of malnutrition, are not evident in the case under discussion, in which the delay of puberty seemed to me, as I tried to say in my first letter, "hormonal" in origin.

The statement of the writers that in hypopituitarism the glomerulosa may be markedly atrophic is, I fear, not really relevant to my point about the effect of hypophysectomy on the cortex and on mineral metabolism. It is to be remembered that Professor van Buchem's cases,[3] where the glomerulosa and reticularis were found more atrophic than the fasciculata, were cases of Sheehan's syndrome—i.e., a *chronic* hypofunction of the whole adenohypophysis. This is in contrast with the fact that hypophysectomy results in atrophy which starts from the reticularis and then affects the fasciculata, leaving the glomerulosa least involved or, as happens in rats, completely untouched.[4 5] What the mechanism is by which a chronic disease of the adenohypophysis can invert this effect on the cortex and produce such a marked glomerulosal atrophy, I cannot say.

The glucose curve was indeed "delayed," if not "lagging," and I shall be most interested to read the paper, when it appears elsewhere, showing this to be a combined effect of aldosterone and potassium on carbohydrate metabolism.

The main point in my first letter was to suggest that Professor van Buchem's case could offer no really reliable

1. Brokaw, A. *Amer. J. Physiol.* 1953, **172**, 333.
2. Selye, H. Textbook of Endocrinology. Montreal, 1949; p. 801.
3. van Buchem, F. S. P. *Acta Endocr., Copenhagen*, 1955, **19**, 165.
4. Soffer, L. Diseases of the Endocrine Glands. London, 1956 p. 238.
5. Greep, R. O., Deane H. W. *Ann. N.Y. Acad. Sci.* 1949, **50**, 596.

information about what happens in a normal adrenal cortex and that, therefore, the hypothesis that the normal fasciculata is equally concerned in the production of aldosterone is deprived of much of its weight. I believe this point still holds.

The National Hospital,
Queen Square,
London, W.C.1. G. M. JACOBIDES.

THYROIDECTOMY AND THE RECURRENT LARYNGEAL NERVES

SIR,—Mr. Rundle's letter (Sept. 8) raises again the question of litigation in connection with surgical technique. It would be bad if his dogmatic statements were allowed to pass as universally accepted opinion. It is doubtful if the technique described is in fact "accepted in almost all of the leading clinics." The frankness of the paper by Roy et al.[1] was refreshing, and it remains for Mr. Rundle to produce a comparable series of thyroidectomies in which there has been an adequate independent number of postoperative examinations of the vocal cords.

Wide divergence of opinion was expressed in a discussion at the Royal Society of Medicine on this question of deliberate exposure of the recurrent laryngeal nerve.[2] There can surely be no technical manœuvre that is exclusively correct, and in supporting our claims for the superiority of one particular method we must avoid placing in jeopardy those who differ from us.

In this connection what really matters is not the recurrent laryngeal nerve (since the paper quoted has shown that even if the nerve is damaged there may be perfect voice recovery) but the over-all effect of the operation on the voice. Present investigations show that a considerable number of patients who undergo thyroidectomy suffer a reduction of voice range. The loss of a few top notes without damage to the recurrent laryngeal nerve is just as important to the patient, though it may appear to be of less significance to the surgeon. Wide exposure of the gland inevitably involves division of the strap muscles and interference with laryngeal movement. Minor damage to the cricothyroid may be far more serious than bruising of the recurrent laryngeal nerve.

Deliberate exposure of both recurrent laryngeal nerves is not a guarantee of a perfect post-thyroidectomy voice; nor, in my opinion, should such a manœuvre be regarded as a legal necessity.

London, W.1. D. F. ELLISON NASH.

Public Health

Abuse of Amphetamine

A RECENT report[3] by the W.H.O. expert committee on drugs liable to produce addiction speaks of an addiction which is not yet considered to be of international significance but which is very serious in certain parts of the world—namely, the abuse of amphetamine, popularly known as "wake-amine." The committee had before it a memorandum on the situation in Japan. The number of misusers of amphetamine in Japan has risen steeply since 1948. In May, 1954, 7·2% of 127,142 persons interviewed had taken amphetamine and 1·8% were abusing it. In May and June of the same year 10,148 people were taken into custody because of offences under a law aimed at controlling the drug; of these offenders, 5320 were found to be addicts. Addiction was commonest in the teens and twenties, and in one city about 5% of those between 16 and 25 were addicts.

In the years immediately after the late war amphetamine was available to anyone in Japan, and it was taken by students who wanted to be more effective in study or in sports, by night workers, and by some people for curiosity or because they wanted to enjoy night life. In recent years, however, there have been more cases in which addicts were first induced to take the drug by the solicitation of illegal distributors. Other factors which stimulated abuse of amphetamine in Japan were the large military stock of the drug which was readily available immediately after the surrender, the spiritual collapse of the people, and the indifference of family and community to education of the young during the post-war period.

Addicts give themselves amphetamine chiefly by the intravenous or subcutaneous route in doses which may be as high as 600 mg. a day. Some also take hypnotic or narcotic drugs in an effort to regain the sleep-wakefulness balance which has been upset by amphetamine. Physical dependence on the drug is not very pronounced, and prompt prohibition of the taking of the drug is therefore the first step in treatment. In fact, it is considered illegal in Japan to administer amphetamine to the addict for therapeutic purposes. The Japanese government has taken vigorous steps to curb the addiction and restrict the supply of the drug; and the UNESCO commission on narcotic drugs has urged other governments to do the same.

Poliomyelitis

Uncorrected notifications of poliomyelitis in England and Wales in the week ended Sept. 8 were as follows: paralytic 37 (53), non-paralytic 68 (71); total 105 (124). This is a decrease of 19 compared with the previous week, the figures for which are in parentheses.

Obituary

JOHN LAWRENCE GAMMIE
M.B. Aberd., D.P.H.

Dr. Gammie, a depute medical officer of health for Edinburgh and lecturer in preventive medicine in the university, died on Aug. 30 at the age of 52. He was born at Macduff and studied medicine at the University of Aberdeen. After graduating M.B. in 1926 he held house-appointments in Aberdeen at the city fever hospital and at Woodend Hospital. In 1928 he took the D.P.H. He joined the Edinburgh public-health department in 1932 as senior medical officer and depute tuberculosis officer, and was appointed junior depute medical officer of health in 1937. In 1939 he willingly undertook the duties of medical officer in charge of the Edinburgh civil-defence casualty service. He was appointed, in 1946, a lecturer in the university department of public health and social medicine, and he was also lecturer in health education to the Moray House Training College for Teachers. As depute medical officer of health he made a particular study of environmental hygiene and infectious-disease control and was often consulted by family doctors throughout the city. He leaves a widow, who is also a doctor, and a young son.

Two of his colleagues write:

John Gammie's brusque, sometimes even peremptory, manner made him often misunderstood, but underneath that somewhat forbidding exterior there beat a warm and generous heart, a heart moreover that preferred to do its kindly deeds by stealth rather than openly. As a colleague he was ever willing and helpful, his advice being based on a wide knowledge of his chosen subject, and as a teacher his lectures were models of clarity and incisiveness. Medicine, however, was not his only interest. He was a lover of good literature and possessed the gift of apt quotation, and his knowledge of the history of dress was considerable. He had strong leanings towards mathematics and his opinions on statistical matters concerned with public-health work revealed sound judgment. His least-known side was probably his curiosity about food, and in his bachelor days he often recounted to us with a twinkle in his eye the successful and unsuccessful experiments he had conducted with this and that dish. We have lost not only a versatile colleague but also one who fully measured up to the true meaning of the word friend.

H. E. S., another colleague, describes him as a man with outstanding gifts of mind, and continues:

His wide knowledge of medicine and of affairs in general, together with a pawky Aberdonian wit, made him a clear, informative, and interesting lecturer and speaker and a most agreeable and entertaining companion and colleague. Those

1. Roy, A. D., Gardiner, R. H., Niblock, W. M. *Lancet*, 1956, i, 988.
2. *Proc. R. Soc. Med.* 1955, **48**, 437.
3. *Wld. Hlth. Org. techn. Rep. Ser.* 1956, **102**.

who knew him best will always remember him as a loyal friend who inspired feelings of affection and regard of an unusual degree and depth. His personal qualities were not always revealed on short acquaintance, but all who worked with him were quick to recognise his generous nature and kindness of heart. Not many, however, knew of the help and service he gave quietly and unobtrusively to those who came to him in trouble or difficulty. For them he never spared himself in time, thought, or material assistance, and not a few present in the large congregation gathered to pay their last respects must have looked back with deep gratitude to the help and guidance given them by John Gammie when things seemed dark and hopeless.

DONALD STAFFORD MATTHEWS

M.B. Edin., F.R.C.S.E., M.R.C.O.G.

Dr. Matthews was a New Zealander who came to Edinburgh to study medicine. After graduating M.B. in 1942, he spent the rest of the war in the Navy in H.M.S. *Achilles*. On demobilisation he took up an appointment in the department of obstetrics and gynæcology at the Postgraduate Medical School at Hammersmith to work for the M.R.C.O.G., which he obtained in 1948. The same year he took the F.R.C.S.E., and a few months later he was appointed lecturer in the department of obstetrics and gynæcology at University College, Ibadan, Nigeria.

In 1950 he took up an appointment in private practice in Calcutta, and in 1954, in fulfilment of his constant desire for travel and excitement, he served as medical officer to the reconnaissance party that paved the way for the successful conquest of Kangchenjunga. He left Calcutta this year and was doctor to the successful British Huagaruncho Expedition. He died at the age of 38 in a hotel at Lima, Peru, on Aug. 27.

A. H. C. W., who was his colleague at Hammersmith and in Nigeria, writes:

At Ibadan Matthews made invaluable contributions in the difficult task of setting up a new medical faculty. He was a tower of strength in his own department and handled vast clinics with efficiency and conscientiousness; and he also organised and ran the venereal-diseases clinic. He was one of the most popular members of the staff and was held in high esteem by the students. He endeared himself to his patients and the citizens of Ibadan, and was one of the few who learnt their language. As a result they loved to hear him converse with them. He was always cheerful, in robust health, and generous almost to a fault. His book *Medicine my Visa*, the proofs of which he was correcting, will reveal his interests and his experiences in his wide travels. Donald was a walking encyclopædia. He had a keen brain, with many constructive ideas for the advancement of his subject. Few men could have played and worked as hard as he did.

Appointments

DAVIS, A. R., M.R.C.S.: deputy M.O.H., Rhondda.

* DONALD, A. B., M.B. Glasg., D.M.R.E.: whole-time consultant radiologist, Durham and North West Durham H.M.C. areas.

GRANT, BRENDA, M.B. Lpool: registrar in psychiatry, Bristol mental hospitals.

INGRAM, F. L., M.R.C.S., L.D.S. R.C.S., D.M.R.D.: consultant radiologist, dental department, Guy's Hospital, London.

PEARSON, S. G., M.B. Leeds, F.R.C.S., D.M.R.T.: consultant radiotherapist, Royal Infirmary and the Western Hospital (General), Edinburgh.

PINES, ARNOLD, M.D. Camb., M.R.C.P.E.: whole-time senior hospital M.O., Edinburgh Royal Victoria and associated hospitals.

THOMAS, T. D. LL., M.B. Lpool, D.P.H.: deputy M.O. for Cardiganshire and M.O.H. for Aberystwyth, Cardigan, and Lampeter.

THORNE, M. G., M.D. Camb., M.R.C.P.: consultant physician, Torbay Hospital, Torquay.

TURGEL, IRENE, M.D. Berlin: part-time consultant psychiatrist, child-guidance services, Bradford and Huddersfield.

WALLACE, H. E. R., M.B. St. And., D.P.M.: whole-time consultant psychiatrist and deputy physician-superintendent, De la Pole Hospital, Willerby.

WILLIAMS, CATRIN M., M.B. Wales, F.R.C.S.E.: consultant E.N.T. surgeon, Clwyd and Deeside H.M.C.

* Amended note.

Sheffield Regional Hospital Board:

BERLINER, FRITZ, M.D. Berlin: whole-time consultant psychiatrist, Pasture Hospital, Mickleover, near Derby.

CHAPEL, J. A., O.B.E., M.D. Edin.: part-time M.O., based on Hillcrest Hospital, Leicester.

CROWTHER, J. S., M.D. Lond., M.R.C.P.: whole-time assistant chest physician, Chesterfield and North Derbyshire area.

LOMAX, WILFRED, M.D. Leeds, D.P.H.: senior assistant psychiatrist, St. Catherine's Institute, Doncaster.

MORGAN, MARJORIE A., M.B. Madras, D.P.M.: whole-time senior assistant psychiatrist, Bracebridge Heath Hospital, Lincoln.

Notes and News

FOOD IN MENTAL HOSPITALS

OVER a year ago [1] Mr. Harington Hawes pointed out in our columns that "The tradition that mental patients need only one substantial meal in the day, and that most of them are oblivious to what they eat or how their food is served, dies hard." Hope of the tradition's approaching demise is strengthened by the growing and practical concern with this problem which is being shown at the Ministry of Health. Last May the Minister announced that this year he was making a special allocation of £500,000 to help hospitals to improve their kitchens and buy more up-to-date equipment. Mr. Hawes made it clear that in many hospitals over-large central kitchens, poor equipment, and lack of staff made the service of appetising meals impossible even where the hospital committee and the staff were most anxious to improve the patients' food. According to his estimate of the need, the Minister's allocation will enable only a modest start to be made on what must be a long-term programme.

Apart from kitchens and equipment meals depend on the ingredients used, and the figures and menus given by Mr. Hawes suggest that in mental hospitals too little money is being spent on the food itself. The letter which the Minister of Health sent last week to regional hospital boards and hospital management committees considers that here an "immediate start" might be made. The nutritive value of the diet could, the Minister suggests, be raised without staff changes, alterations to buildings, or additional equipment, by:

improving the quality of dishes prepared by substituting for poor recipes other recipes with the normal proportion of ingredients. This will usually mean increasing milk in milk-puddings and sauces; fats and sugar in pastries and puddings; meat and fish in made-up dishes, stews, &c.;

reviewing the amount of milk per patient per week which should not be less than 5¼ pints, exclusive of that required for sick diets and staff;

increasing the issues per head per week of meat and other protein-containing foods, fresh vegetables (except potatoes), and fruit.

The Minister would also like to see the range and variety of dishes improved and the service of a substantial cooked or savoury dish at a later evening meal. But for these improvements he agrees that more staff and better facilities would often be needed. In hospitals where the modernisation of the kitchens is being planned he proposes that adequate roasting and baking equipment should be provided to enable a full and varied dietary to be cooked, and that the boiling capacity, needed only for the older type of diet, should be reduced.

SOCIAL ANTHROPOLOGY AND PSYCHIATRY

AT the Maudsley Hospital, London, on Sept. 14, Dr. Margaret Mead, of the American Museum of Natural History, New York, spoke on the contribution of social anthropology to psychiatry. She defined social or cultural anthropology as primarily concerned with the study of behaviour in living people in situ. Its findings, when a small primitive community was studied, were of value to the psychiatrist in providing a cross-cultural check for hypotheses that were culture-bound. For instance, there was much emphasis nowadays in psychiatric circles on the importance of breast-feeding for the future mental stability of the infant. It was easy for the psychiatrist in Western civilisations to ignore the fact that the vast majority of the world's population still habitually breast-fed its children. The cultural anthropologist could provide many samples of the different responses to breast-feeding and the variations within this general practice. One American psychiatrist, greatly impressed by the importance of breast-feeding, held that breast-feeding in infancy was the reason for the stoicism of a South-Sea island tribe when their large and painful boils were lanced. But social anthropologists could have provided him with plenty of examples of people, breast-fed in infancy, who screamed or ran away when anyone attempted to lance their boils. This sort of negative checking of theory was a valuable corrective to the psychiatrist, who was often unable to distinguish between innate and environmental factors.

In large communities, such as those in which the average psychiatrist worked, he had to be content with sampling, whereas the social anthropologist could study a small community in its entirety, giving to every individual an equal amount of attention and determining the relation of every

1. *Lancet*, 1955, i, 1214.

single person to everyone else in the group. It followed that the anthropologist could offer the psychiatrist understanding only in the field of *learned* rather than *innate* factors in behaviour. He could also help to combat the tendency to emphasise one factor at the expense of another.

The anthropologist saw people in a situation where, for instance, the baby and mother who cannot adapt to breast-feeding had no place, for the baby died. The culture could only keep alive a baby who reacts to breast-feeding within certain limits. In our modern culture, a mother who could not feed her baby used to be labelled a "rejecting mother," but her baby would be bottle-fed and given a "formula" because our culture tolerated a greater range of variabilities. The psychiatrist was vitally concerned with the problem of stretching the limits of redundancy, for he had to help the mentally ill to re-enter the community. It was not only a question of the patient's readaptation to society but of how many mentally ill people the society could tolerate.

The wide variations in human response revealed by the field studies of social anthropologists also broadened the range of our awareness of possible types of behaviour. If this were applied in our educational programmes, we might be able to teach our children in terms of relative rather than absolute values. The way in which we were taught our mother tongue and learned to be human in our own culture determined our future ability to learn a foreign language and to be human in another way. It was easier, Dr. Mead said, to change from one pattern to another if we were taught from the outset that there were other patterns and if we were not brought up to think that our own culture possessed absolute values.

University of London

On Sept. 24 and 25, at 5.15 P.M., at the Royal Free Hospital School of Medicine, 8, Hunter Street, Brunswick Square, W.C.1, Dr. J. H. Comroe, professor of physiology and pharmacology in the University of Pennsylvania, will speak on tests of pulmonary function.

University of Birmingham

Dr. Walter Bauer, Sterling professor of clinical medicine at Harvard and physician-in-chief at the Massachusetts General Hospital, is to be visiting professor of medicine in the University of Birmingham during October.

Queen's University, Belfast

Dr. J. G. Gibson has been appointed to the newly instituted chair of mental health.

Dr. Gibson, who is a graduate of Queen's University, qualified in 1942. After holding house-appointments at the Royal Victoria Hospital and the Belfast Maternity Hospital he visited the United States with a teaching fellowship in psychiatry at Harvard medical school, and he later held a post at Massachusetts General Hospital, Boston. After his return to this country he became senior registrar at the Maudsley Hospital, London. In 1947 he took his M.D. degree and two years later the M.R.C.P. He took the D.P.M. in 1954. At present he is senior lecturer at the Institute of Psychiatry of the University of London and honorary consultant to the Bethlem Royal and Maudsley Hospitals.

Dr. I. J. Carré has been appointed to a lectureship in child health.

Dalhousie University

Dr. W. A. Taylor has been appointed to the chair of pathology in Dalhousie University and director of the division of pathology of the Nova Scotia department of public health.

Dr. Taylor was born at Balloch, and educated at Glasgow and Dumbarton Academies. He graduated B.SC. with first-class honours in physiology in 1942. The same year, with a Rockefeller studentship, he went to America and studied medicine at Stanford University, San Francisco, and at Cornell University, New York. After he returned to Glasgow in 1945 he graduated M.B. and joined the staff of the pathology department of Glasgow University at the Western Infirmary under Prof. D. F. Cappell. In 1947 he became lecturer in pathology there, and he remained at the Western Infirmary until 1955 when he went to Dalhousie as associate professor.

Association of Clinical Pathologists

A meeting of this association will be held at the Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2, on Oct. 4, 5, and 6.

Technology and Industry

On Friday, Nov. 16, at 6.30 P.M., at the London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1, as one of a course of London University extension lectures on this subject, Sir Charles Dodds, F.R.S., will speak on Pharmaceutical Applications of Modern Biochemistry.

Charing Cross Hospital Medical School

The prize-giving of this school will be held at the Mansion House, London, E.C.4, on Friday, Sept. 28, at 3 P.M., when Viscount Kilmuir will give the inaugural address.

Middlesex Hospital Medical School

The annual dinner to past and present students will be held at the Savoy Hotel, London, W.C.2, on Friday, Sept. 28, at 7.30 P.M. Mr. F. W. Roques will be in the chair.

King's College Hospital Medical School

Mr. Norman Barrett will give the Thomas Percy Legg lecture at 4.30 P.M. on Friday, Oct. 12, at this medical school, Denmark Hill, London, S.E.5. He will speak on the Short Œsophagus.

Yorkshire Association of Graduates of Glasgow University

The annual dinner of this association will be held at the Great Northern Hotel, Leeds, on Oct. 6 at 7.30 P.M. Further particulars may be had from Mr. James Wishart, 33, Manor Row, Bradford, 1.

Injury, Compensation, and Employment

The British Council for Rehabilitation is holding a conference on this subject at Tavistock House, London, W.C.1, on Friday, Oct. 12, at 10 A.M. Sir Hugh Griffiths will be in the chair, and other medical speakers will include Dr. C. J. S. O'Malley and Dr. D. C. Norris. Further particulars may be had from the general secretary of the council, Tavistock House (South), W.C.1.

British Epilepsy Association

This association is holding a residential course on epilepsy at Queen Elizabeth College, Campden Hill Road, London, W.8, from Sept. 26 to 29. The speakers will include Dr. Denis Williams, Dr. Denis Hill, Mr. Murray Falconer, Dr. Colin Edwards, Dr. F. H. Tyrer, Dr. Christopher Ounsted, Dr. Desmond Pond, and Dr. Denis Kennedy. Further particulars may be had from the secretary of the association, 136, George Street, W.1.

Teaching Children in Hospital

Local education authorities have been asked by the Ministries of Education and Health to review their arrangements for providing primary and secondary education for children in hospital. In 1955 there were 120 hospital schools in England and Wales, with 6476 children on the roll, and 1425 other children were receiving individual tuition, but the Ministry of Education believes that there are "still some educable children in hospital for whom no provision has been made." The Ministry of Health has asked hospitals, where there is no hospital school or regular teaching group, to inform education authorities about the admission of any child who is likely to remain in hospital and will be well enough for some teaching. Regional hospital boards and boards of governors of teaching hospitals are asked, whenever medical needs and the requirements of their hospital care and treatment permit, to group children together in sufficient numbers to make a special school a practical proposition.

CORRIGENDA: *Estimation of Serum-amylase.*—The laboratory checks mentioned by Dr. S. Shaldon in his article last week (p. 547) were made by the method of King (E. J. King, Micro-analysis in Medical Biochemistry. London, 1946; p. 61).

Familial Incidence of Low Pseudocholinesterase Level.—In early copies of last week's issue the word "relations" appeared erroneously in place of "reactions" in line 6 of the last paragraph of Dr. W. Kalow's letter (p. 576).

Sir Russell Brain, P.R.C.P., has been appointed a trustee of the Ciba Foundation.

Dr. L. Cudkowicz has been awarded the James Hudson Brown fellowship in medicine at Yale University for 1956–57.

The kymograph tracings in the article by Dr. Galley and Dr. Rooms (June 23, p. 992) were made on an apparatus bought from a grant by the University of London Central Research Fund Committee.

The committee appointed in 1954, under the chairmanship of Sir Stewart Duke-Elder, to review standards for trial case lenses and the method of measuring lens powers has now reported (Trial Case Lenses: Report of a committee appointed by the Minister of Health. H.M. Stationery Office. Pp. 25. 1*s.* 9*d.*).

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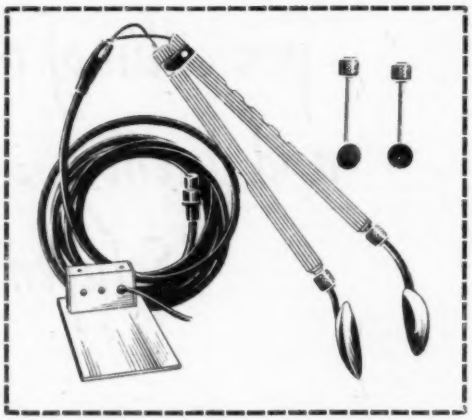

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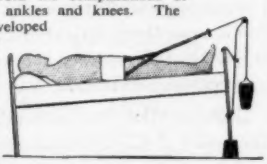

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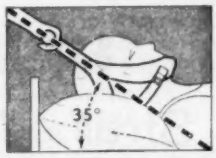

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Wednesday, 24th Oct.	Encephalomyelitis	Dr. P. SANDIFER
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Wednesday, 7th Nov.	Spinal Abscesses	Dr. M. KREMER
Wednesday, 14th Nov.	Intracranial Abscesses	Mr. VALENTINE LOGUE
Wednesday, 21st Nov.	Syphilis of the Central Nervous System, I	Dr. J. ST. C. ELKINGTON
Wednesday, 28th Nov.	Syphilis of the Central Nervous System, II	Dr. J. ST. C. ELKINGTON
Wednesday, 5th Dec.	Cerebral and Spinal Thrombophlebitis	Dr. M. J. MCARDLE
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At the close of the proceedings in Nuffield House, tea will be served in the Medical School.

Past and present students of the Medical School are cordially invited to attend the lecture and also an Informal Conversazione which is to be held the same evening in the Medical School.

Further particulars and tickets for these functions may be obtained from the Sub-Dean, The Medical School, Birmingham, 15. A. P. THOMSON, Dean.

KING GEORGE V HOSPITAL FOR DISEASES OF THE CHEST

GODALMING

A CLINICAL COURSE will be held on 3RD, 4TH, and 5TH OCTOBER. Fee £3 3s. (excluding accommodation).

Further information from the Secretary, Tuberculosis Educational Institute, Tavistock House North, Tavistock-square, London, W.C.1.

THE UNIVERSITY OF LIVERPOOL

DEPARTMENT OF STUDIES IN PSYCHOLOGICAL MEDICINE

POSTGRADUATE INSTRUCTION IN PSYCHOLOGICAL MEDICINE

A COURSE designed for those studying for a Diploma in Psychological Medicine will commence in JANUARY, 1957. Instruction will be part-time and will occupy approximately 3 half-days a week during 6 academic terms ; 3 terms being devoted to Part I and 3 terms to Part II. Students may enrol for either part separately, but, except in special circumstances, will not be permitted to study for both parts concurrently.

Fees : £12 12s. per term or £70 for the whole course.

Further particulars may be obtained from the Director, Department of Studies in Psychological Medicine, 77, Bedford-street South, Liverpool, 7, to whom application for admission to the course should be sent as soon as possible.

THE UNIVERSITY OF LIVERPOOL

RADIOLOGY

The University of Liverpool provides a FULL-TIME COURSE of 2 academic years leading to a DIPLOMA IN RADIOLOGY which can be taken in either Radio-diagnosis or Radiotherapy (D.M.R.(D.) Liverpool or D.M.R.(T.) Liverpool), and which is open to graduates of approved medical schools. The course (which begins in OCTOBER each year) allows a candidate to hold suitable approved hospital appointments during the second year, and covers the regulations required by the Conjoint Board. The fee for the full 2-year course is £63. The degree of M. Rad. may, after report by the Faculty, be conferred on holders of the D.M.R.(D.) or (T.) Liverpool under certain conditions.

Applications for further information should be addressed to the Dean of the Faculty of Medicine.

STANLEY DUMBELL, Registrar.

INSTITUTE OF NEUROLOGY (Queen-square)

2 COURSES OF CLINICAL DEMONSTRATIONS, open to Postgraduates, will be held at The National Hospital, Queen-square on WEDNESDAYS at 4 P.M. from 10TH OCTOBER to 19TH DECEMBER, 1956, inclusive, and on SATURDAYS at 10.30 A.M. from 6TH OCTOBER to 15TH DECEMBER, 1956, inclusive.

The fee for attending either of these courses is 2 guineas.

Application for a ticket should be made to The Dean, Institute of Neurology (Queen-square), The National Hospital, Queen-square, W.C.1, and a remittance to cover the fee enclosed. Only postal applications will be considered.

THE ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE

THE DIPLOMA IN PUBLIC HEALTH
THE DIPLOMA IN INDUSTRIAL HEALTH

The next COURSES OF INSTRUCTION for the above Diplomas will commence on 28TH SEPTEMBER, 1956. Tuition may be taken whole-time or part-time.

Prospectuses, enrolment forms and full details may be obtained from the Secretary, 28, Portland-place, London, W.1 (Telephone : LANgham 2731 2).

DICKINSON SCHOLARSHIPS

Applications are invited for a Research Scholarship in Medicine or Surgery value £150.

Candidates must be graduates of any University who have taken their full course of instruction in medicine and surgery at the University of Manchester and at the Manchester Royal Infirmary.

Copies of the regulations governing the Scholarships may be obtained from the undersigned, to whom 6 copies of application should be sent not later than 30th September, 1956.

G. H. TAYLOR,
Secretary to the Dickinson Scholarship Trustees.
Manchester Royal Infirmary, Manchester, 13.

TANCRED'S STUDENTSHIPS

DIVINITY : MEDICINE : LAW
£100 p.a. each. For men only

The Governors propose to elect 1 Student in Divinity at Christs College, Cambridge, on the result of the Scholarship Examinations to be conducted in DECEMBER, 1956, by the Queens, Christ's, St. Johns, Emmanuel and Sidney Sussex Group of Colleges in the University of Cambridge.

Candidates must have been born in England, Scotland or Wales, and be members of the Church of England and unmarried ; they must also be within the ages of 17 and 22 years.

Candidates should in addition to making the necessary arrangements with the Managers of the above Scholarship examinations send in a Petition to the Clerk to the Tancred Foundation by 1st November, 1956.

Further announcements relating to the Physic and Law Studentships awarded by this Foundation will appear in February and April, 1957.

Apply for further particulars and form of Petition stating kind of Studentship and mentioning this paper to the Clerk, R. M. C. HOWARD, Esq., D.S.O., 28, Lincoln's Inn-fields, London, W.C.2.

THORACIC SURGERY

TRAVELLING FELLOWSHIP TO AMERICA

Applications are invited from people of Senior Registrar or Consultant status working in Thoracic Surgery for a Fellowship in America for 1 year, commencing JULY, 1957. The Fellowship is provided through the generosity of the American Association for Thoracic Surgery. Further particulars are available if desired.

Applications, together with the names of 2 referees, should be sent before 14th October, 1956, to—

J. LEIGH COLLIS, Honorary Secretary,
Society of Thoracic Surgeons.
15, Highfield-road, Edgbaston, Birmingham, 15.

DENTAL AND MEDICAL SOCIETY FOR THE STUDY OF HYPNOSIS

The above society will hold a STUDY GROUP on THE THEORY AND PRACTICE OF HYPNOSIS beginning on WEDNESDAY, 3RD OCTOBER, 1956. 2-hour lecture-demonstrations will begin at 7.15 P.M.

AN INTENSIVE WEEKEND COURSE will be held on 24TH and 25TH NOVEMBER for members who live too far away from London to attend the full course.

A fee is charged for these Study Groups.

The Society is prepared to send a team of lecturers and subjects to any locality in Great Britain to give an intensive weekend course provided that sufficient Medical and Dental practitioners are willing to attend.

Further details may be obtained from the Secretary, Mr DAWSON WATTS, 22, Gordon-road, Ealing, W.5.

THE POSTGRADUATE COMMITTEE IN MEDICINE
THE UNIVERSITY OF SYDNEY

MEDICAL POSTGRADUATE TRAINING FELLOWSHIPS

Applications are invited from medical graduates for a Fellowship which may be held in any subject in the medical curriculum.

These training Fellowships have been established with the general object of advancing the art and science of medicine by means of postgraduate study, training and research and with the particular object of enabling graduates in medicine to obtain experience and training in medical research. They may be held wholly or partly in Australia or abroad, may include Fellowships for primary research and of academic intent, fellowships for vocational study and training and fellowships for a combination of such purposes.

Appointment will be for 1 year but may be renewed for a second or third year. The salary will be up to £1200 for a single man and £1500 for a married man, which will include fares and allowances.

Applications will close on 30th November, 1956, and should be made to the Honorary Director, The Postgraduate Committee in Medicine, 131, Macquarie-street, Sydney, to whom intending applicants must first communicate so that full particulars of the Fellowship and details of the method of application may be obtained.

SOCIETY OF APOTHECARIES OF LONDON

DIPLOMA IN INDUSTRIAL HEALTH

The next Examination will begin on MONDAY, 3RD DECEMBER, 1956. The following Examination will be held in July, 1957.

For Regulations apply Registrar, Apothecaries' Hall, Black Friars-lane, London, E.C.4.

THE UNIVERSITY OF LIVERPOOL. Applications are invited for a post in the Department of Physiology, from medically qualified candidates, as an ASSISTANT LECTURER at an initial salary of £700 p.a., or as a LECTURER at an initial salary within the range £1000–£1200 p.a., according to qualifications and experience, or from non-medically qualified candidates, as an Assistant Lecturer at an initial salary of £550 p.a. (in special circumstances £600 p.a.), or as a Lecturer at an initial salary within the range £650–£800 p.a., according to qualifications and experience.

Applications, stating age, academic qualifications, and experience, together with the names of 3 referees, should be received not later than 6th October, 1956, by the undersigned, from whom further particulars of the conditions of appointment may be obtained. STANLEY DUMBELL, Registrar.

UNIVERSITY OF BRISTOL. The University invites applications for the post of LECTURER IN OBSTETRICS AND GYNÆCOLOGY. Salary £1200–£100–£1750 p.a. according to qualifications and experience, together with superannuation and children's allowances. The successful candidate will be granted an honorary contract as Senior Registrar with the Board of Governors of the United Bristol Hospitals and the South-Western Regional Hospital Board.

Applications (20 copies), including the names of 3 referees, should reach the Registrar, from whom further particulars may be obtained, not later than 6th October, 1956.

UNIVERSITY OF EDINBURGH. Medical Physics Unit. Applications are invited for the post of DIRECTOR of the Medical Physics Unit with status of Senior Lecturer. This Unit is being established jointly by the University and the South-Eastern Regional Hospital Board, Scotland. Salary scale £1750–£100–£2250 p.a., with superannuation benefit and, where applicable, family allowance.

Further particulars may be obtained from the Secretary to the University, Old College, South Bridge, Edinburgh, with whom applications, giving the names of 3 referees, should be lodged by 1st November, 1956.

UNIVERSITY OF OXFORD. Department of Pathology, RADCLIFFE INFIRMARY. Applications are invited for the post of SENIOR RESEARCH OFFICER IN NEUROPATHOLOGY, for a period of 5 years in the first instance. Salary scale £1000–£50–£1700; F.S.S.U. and family allowance. The successful candidate will be expected to take up duties in the early part of Michaelmas Term, 1956. Preference would ordinarily be given to candidates with experience in neuropathology, but favourable consideration would be given to candidates experienced in general morphological pathology who would wish to specialise in neuropathology. In addition to some teaching duties and facilities for research, the duties include the investigation of the neurosurgical and neurological specimens of the United Oxford Hospitals.

Applications, with the names of 2 referees, should be sent by 6th October to Dr. A. H. T. ROBB-SMITH, Department of Pathology, Radcliffe Infirmary, Oxford, from whom further particulars may be obtained.

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG, SOUTH AFRICA. Applications are invited for appointment to a post of SENIOR LECTURER and a post of LECTURER on the staff of the University's Department of Physiology, Medical School. Candidates with a medical qualification or a higher degree in experimental physiology and/or biochemistry are eligible for appointment. The salary scale attached to the post of Senior Lecturer is £1100–£50–£1450 and to the post of Lecturer £850–£50–£1150. In addition, a married man will receive cost-of-living allowance at the rate of £234 p.a. The commencing salary will depend upon qualifications and experience in teaching and research. Membership of the Provident Fund is compulsory and involves a contribution at the rate of 7% of the salary paid, the Government and the University together contributing an equal amount. Membership of the Staff Medical Aid Fund is compulsory in the case of an officer who is found eligible for membership.

Applicants are advised to obtain a copy of the information sheet regarding the above vacancies from the Secretary, Association of Universities of the British Commonwealth, 36, Gordon-square, London, W.C.1. Applications close in South Africa and London on 31st October, 1956.

UNIVERSITY COLLEGE, Ibadan, Nigeria. Applications are invited for SENIOR LECTURESHIP IN RADIOLOGY. The appointee will also be Director of the Clinical Department of Radiology in the new teaching hospital. Initial appointment 3 years. Salary scale £1850–£100–£2450 p.a. Allowance up to 3 children, £50 p.a. per child resident in Nigeria and £100 p.a. per child resident elsewhere. Part furnished accommodation at rent up to 7·7% of salary. Passages for appointee, wife and up to 3 children under 11 years on appointment, overseas leave and termination. F.S.S.U. Outfit allowance £60.

Detailed applications (10 copies), naming 3 referees, by 5th October, 1956, to Secretary, Senate Committee on Colleges Overseas in Special Relation, University of London, Senate House, London, W.C.1, from whom further particulars may be obtained.

Hospital Services : Senior Appointments

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.

(1) CONSULTANT PHYSICIAN (whole-time), St. Pancras Chest Clinic, 26, Margaret-street, W.1. Good general medical experience and special experience in chest diseases essential. The Physician appointed will have charge of 47 Beds at Whittington Hospital, Highgate Wing. Post vacant 18th March, 1957.

Applications before 22nd October, 1956.

(2) ASSISTANT PHYSICIAN in Physical Medicine (2 half-days a week), Senior Hospital Medical Officer grade, King Edward Memorial Hospital, Ealing (151 Beds).

Applications before 26th October, 1956.

Clinic and Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time CONSULTANT ANÆSTHETIST for the Wandsworth Group of hospitals. Duties mainly at St. James' Hospital, Balham, S.W.12.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 20th October, 1956. Applicants may visit Hospital by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Part-time CONSULTANT ANÆSTHETIST (6 half-days per week) for the Fulham and Kensington Group of hospitals, duties mainly at St. Mary Abbots Hospital, W.8.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 20th October, 1956. Applicants may visit Hospital by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Part-time CONSULTANT ANÆSTHETIST (2 half-days per week) for the St. Helier Group of hospitals. Duties mainly at the Nelson Hospital, S.W.20.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 20th October, 1956. Applicants may visit Hospital by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time CONSULTANT PSYCHIATRIST at Springfield Hospital, S.W.17 (2000 Beds, including male and female neurosis units). The appointment includes both intramural and extramural duties. Candidates should have D.P.M., and a higher medical qualification and have had extensive experience in all branches of psychiatry. Resident quarters available for a single person.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 20th October, 1956. Applicants may visit Hospital by local arrangement.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Royal ORTHOPÆDIC HOSPITAL, BIRMINGHAM. (242 Beds.) Whole-time Locum Tenens ASSISTANT ORTHOPÆDIC SURGEON (Senior Hospital Medical Officer). Duties also at associated hospitals and clinics. Vacant minimum 4 months. Salary 31½ guineas per week.

Applications to Senior Administrative Medical Officer, 10, Augustus-road, Birmingham, 15.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Part-time CONSULTANT GERONTOLOGIST (9 notional half-days weekly). Duties in the Wolverhampton Group, especially at New Cross Hospital (5 notional half-days weekly) and Walsall Group at St. John's Hospital (4 notional half-days weekly). Experience specialty and higher qualification required.

Applications (15 copies), stating age, qualifications, experience, nationality and naming 3 referees, to Secretary, 10, Augustus-road, Birmingham, 15, by 8th October, 1956.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. ASSISTANT CHILD PSYCHIATRIST (whole-time) in the Cambridge Area. Duties will be predominantly at the Cambridge Child Psychiatric Clinic and branch clinics in the area and by agreement with the Board of Governors will include work in the Psychiatric Outpatient Department of Addenbrooke's Hospital. Wide experience and higher qualification necessary. Salary scale £1575–£2025.

Applications (8 copies), stating age, experience and the names of 3 referees, to Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 1st October, 1956. Candidates invited to visit by arrangement with Consultant Child Psychiatrist, Chesterton Hall, Chesterton-road, Cambridge.

LEEDS REGIONAL HOSPITAL BOARD.
Whole-time CONSULTANT PSYCHIATRIST, specialising in Mental Deficiency, required for duties mainly at Westwood Hospital (520 Beds) and Ashfield House (50 Beds), Bradford, and associated with Stansfield View Hospital, Todmorden (160 Beds). Other duties may be required in the Halifax, Bradford (A), (B) and Bingley, Keighley, Skipton and Settle Groups. The person appointed will be Physician-Superintendent of the above-named hospitals and will be required to reside in Bradford. The duties include those of Medical Arbiter for the Mental Deficiency Area Admission Bureau, together with advising the Local Health Authorities on clinical aspects of mental deficiency as required. Applicants should hold the D.P.M., and have had experience in mental deficiency.

Applications (12 copies), stating age, qualifications and details of appointments held showing dates, with the names and addresses of 3 referees, to the Secretary, Park-parade, Harrogate, by 20th October, 1956.

MANCHESTER REGIONAL HOSPITAL BOARD.
(*a*) Whole-time CONSULTANT GROUP PATHOLOGIST, North and Mid-Cheshire Group of hospitals, mainly at Altrincham General Hospital, near Manchester. Existing laboratory being improved and extended. Good training and experience in all branches of hospital pathology essential. 3rd October, 1956.

(*b*) Part-time (8 half-days weekly) CONSULTANT E.N.T. SURGEON to North and Mid-Cheshire Hospitals (about 4 sessions, mainly at Altrincham General Hospital E.N.T. Department) and Manchester Ear and Wythenshawe Hospitals (2 sessions each). Wide experience and higher qualifications essential, appointee to live in Altrincham area. 5th October, 1956.

(*c*) Whole-time ASSISTANT ORTHOPÆDIC SURGEON (Senior Hospital Medical Officer) to the Burnley and District Group of hospitals, mainly at the Victoria Hospital. Special experience required in the treatment of orthopædic cases, fractures and trauma, higher qualification desirable. Appointee will work under direction of Consultant Orthopædic Surgeon. 1st October, 1956.

Application forms from the Senior Administrative Medical Officer to the Board, Cheetwood-road, Manchester, 8, to be returned by dates stated.

NEWCASTLE REGIONAL HOSPITAL BOARD. St. GEORGE'S HOSPITAL, MORPETH. (1256 Beds.) ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer) whole-time, resident. Candidates should normally hold a D.P.M. but applications will be considered from candidates with no previous practical experience in psychiatry who hold a higher qualification, have had wide experience in general medicine, including Senior Registrar posts, and intend to obtain a D.P.M. and specialise in psychiatry. Full particulars from Medical Superintendent.

Applications, with names and addresses of 3 referees, to Regional Psychiatrist, Newcastle Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

SCOTLAND. NORTHERN REGIONAL HOSPITAL BOARD. Applications are invited for the whole-time post of ASSISTANT ANÆSTHETIST (Senior Hospital Medical Officer grade) based on the Inverness Hospitals. Candidates should have a higher qualification in anæsthetics.

Schedules of application and further particulars may be obtained from the undersigned, with whom applications should be lodged by 15th October, 1956.

A. M. FRASER, M.D.,
Secretary and Administrative Medical Officer.
Office of the Northern Regional Hospital Board,
Raigmore, Inverness.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the whole-time appointment of CONSULTANT RADIOTHERAPIST at the Royal Infirmary and the Western General Hospital, Edinburgh.

Applications, giving particulars of age, qualifications and previous experience, together with the names of 3 referees, should be sent to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 13th October.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the post of Whole-time PHYSICIAN within the salary range £1575–£2025 p.a. Initially duties will mainly be with the Medical Unit in West Fife, based on the Northern Hospital, Dunfermline. The successful applicant, however, will be expected to develop a hospital geriatric service for the whole County of Fife, and it is expected that this duty will eventually absorb the whole of the time of the post. Experience in geriatrics is therefore essential.

Applications, giving particulars of age, qualifications and previous experience, together with the names of 3 referees, should be sent to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 20th October, 1956.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time SENIOR ASSISTANT PSYCHIATRIST required for Saxondale Hospital, Radcliffe-on-Trent, Notts. House available. Salary scale £1575–£50–£2025.

Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 20th October, 1956.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Part-time CONSULTANT ANÆSTHETIST (7 half-days per week) for the Redhill (Surrey) Group of hospitals. Successful candidate will be expected to reside within the Group area.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 20th October, 1956. Applicants may visit Hospitals by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time CONSULTANT PSYCHIATRIST at Long Grove Hospital, Epsom, Surrey. Candidates should possess D.P.M. and a higher medical qualification. Wide experience of psychiatry essential with special emphasis on modern mental hospital practice, outpatient work and social psychiatry.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 20th October, 1956. Applicants may visit Hospital by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time PHYSICIAN-SUPERINTENDENT AND CONSULTANT PSYCHIATRIST at Warlingham Park Hospital, Surrey. Candidates should possess D.P.M. and a higher medical qualification, and should have wide experience in psychiatry and a knowledge of medical administration. A house is available.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 20th October, 1956. Applicants may visit Hospital by local arrangement.

NEW ZEALAND. THAMES HOSPITAL BOARD, THAMES, NEW ZEALAND. Applications are invited for the position of Whole-time MEDICAL SUPERINTENDENT of the Thames Hospital Board. Applicants must be registered, or entitled to be registered, as medical Practitioners in New Zealand. Surgical experience and a higher qualification in surgery is necessary. Salary, in accordance with the Hospital Employment Regulations, will be either of the following scales—£NZ1700 p.a.–£NZ2000 p.a. or £NZ2000 p.a.–£NZ2300 p.a. Within these scales the commencing rate and the maximum rate will be as determined by the Medical Officers' Salaries Grading Committee in accordance with the qualifications and experience of the appointee. Residential accommodation is available at a rental of £NZ110 p.a.

Conditions of appointment, application form and an explanatory memorandum are obtainable from the High Commissioner for New Zealand, 415, Strand, London, W.C.2, or the undersigned.

Applications, which should be sent air-mail, addressed to the undersigned, close on Wednesday, 24th October, 1956.

F. HOPKINSON, Secretary.

P.O. Box 53, Thames, New Zealand.

WESTERN AUSTRALIA. ROYAL PERTH HOSPITAL. Applications are invited for the full-time post as STAFF RADIOTHERAPIST who will work under the direction of the Honorary Radiotherapists. Salary within the range of £A2360–£A2540 p.a. according to qualifications and experience, and provided the applicant has the Diploma of Radiotherapy or the equivalent. Applicants without a complete Diploma will receive a salary of £A2097 p.a. The Royal Perth Hospital is the main Teaching Hospital associated with the University of Western Australia. It has more than 600 Beds and is extending.

In addition to all relevant personal details, applications must include particulars of qualifications, experience, and the names of 2 referees, and should reach the undersigned on or before 31st October, 1956. JOSEPH GRIFFITH, Administrator.

Hospital Services : Junior Appointments

BATTERSEA GENERAL HOSPITAL, Battersea Park, S.W.11. HOUSE SURGEON/CASUALTY OFFICER (combined post), resident, vacant immediately. House Officer grade, not pre-registration and not recognised for F.R.C.S.

Apply, enclosing copies of 2 recent testimonials, to Hospital Secretary, with whom arrangements can be made to view the Hospital.

BERNHARD BARON MEMORIAL RESEARCH LABORATORIES, QUEEN CHARLOTTE'S MATERNITY HOSPITAL. A REGISTRAR in Pathology is required at the above laboratories. Previous specialised experience is not essential. The successful candidate will have opportunities to work in all departments, will receive special training in serology and later may assist in research work. The post is resident.

Applications to the House Governor at the Hospital on forms obtainable from 339, Goldhawk-road, London, W.6, within 14 days of this advertisement.

BROMPTON HOSPITAL, S.W.3. Applications invited for the following posts :—

NON-RESIDENT HOUSE PHYSICIAN for which there are 3 vacancies, for 6 months from 1st December, 1956. Duties include work in Outpatient Department and wards, also 1 months duty at Frimley as occasion demands. Salary at the rate of £525 p.a.

RESIDENT HOUSE PHYSICIAN to Cardiac Department for 6 months from 1st December, 1956. Duties include work in Outpatient Department and wards. Salary at the rate of £525 p.a.

Applications, stating age, qualifications with dates, nationality and appointment held, together with copies of testimonials, by 6th October, 1956, to—

KENNETH A. F. MILES, House Governor.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. Applications invited for following post-registration posts :—

RESIDENT HOUSE OFFICER in General Medical Department including hæmatology and endocrinology. Vacant 1st November.

RESIDENT HOUSE OFFICER in General Medical and Neurological Department. Vacant 9th November.

RESIDENT HOUSE OFFICER in General Medical and Cardiological Department. Vacant 8th November.

6 months appointments.

Separate applications, with 2 copy testimonials, to Medical Director by 29th September, 1956.

CENTRAL MIDDLESEX HOSPITAL, N.W.10. North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time RESIDENT PATHOLOGICAL REGISTRAR required, 1 year in first instance, to act as Transfusion Officer, assist the Consultant Hæmatologist, and take part in the 24-hour pathological service. Post vacant 15th October. Hospital may be visited by direct appointment.

Application forms from, and returnable to, Group Secretary, Central Middlesex Group Hospital Management Committee, Acton-lane, N.W.10, by 6th October, 1956.

CONNAUGHT HOSPITAL, Walthamstow, E.17. (118 Beds.) Applications are invited for the post of SECOND CASUALTY OFFICER with duties in the Department of Orthopædic and Traumatic Surgery (Senior House Officer grade). Recognised for F.R.C.S. Salary £745 p.a., less £150 p.a. for board, lodging, &c.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Hospital Management Committee, Forest Group, Langthorne-road, E.11.

DREADNOUGHT SEAMEN'S HOSPITAL, Greenwich, S.E.10. CASUALTY AND RECEIVING-ROOM OFFICER (non-resident) required on 22nd October. Post recognised by the Royal College of Surgeons. Salary £745 p.a.

Applications, stating age, nationality, qualifications, and experience, with the names of 3 recent referees, should be sent to the Secretary at the above address not later than 8th October.

DULWICH HOSPITAL (in association with King's College Hospital Medical School for teaching purposes), East Dulwich-grove, London, S.E.22. Applications invited for appointment as SENIOR HOUSE OFFICER (obstetrics and gynæcology). Post vacant 1st November. Recognised for M.R.C.O.G.

Apply, giving age, qualifications and experience, with copy testimonials or names of 2 referees, to Group Secretary, Camberwell Hospital Management Committee, Dulwich Hospital, S.E.22, not later than 5th October.

DULWICH HOSPITAL (in association with King's College Hospital Medical School for teaching purposes), East Dulwich-grove, London, S.E.22. Applications invited for appointment to 2 positions of HOUSE OFFICER (medical duties). Recognised pre-registration posts. Vacant from 1st October.

Apply to Group Secretary, Camberwell Hospitals Management Committee, Dulwich Hospital, S.E.22, as soon as possible, enclosing copy testimonials or names of 2 referees.

EAST END MATERNITY HOSPITAL, 384/398, Commercial-road, London, E.1. (58 Beds.) Applications are invited for the following posts which are recognised for the M.R.C.O.G.

RESIDENT SENIOR OBSTETRICAL OFFICER (Senior House Officer grade).

RESIDENT OBSTETRICAL OFFICER (House Officer, third post).

Posts vacant 1st November, 1956.

Applications, with copies of testimonials, to the Secretary, Stepney Group Hospital Management Committee, Raine-street, Wapping, E.1, by 24th September, 1956.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. A vacancy occurs for RESIDENT SURGICAL OFFICER. Appointment for 6 months, with prospect of renewal. Post graded as Senior House Officer or Registrar, according to qualifications and previous surgical experience.

Applications, stating date of birth, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should reach the undersigned not later than 26th September, 1956. THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. MEDICAL REGISTRAR (Cardiac Department). Applications are invited for this post, which is graded Registrar. Previous experience in cardiology and cardiac catheterisation desirable but not essential. The appointment is for 1 year with eligibility for reappointment.

Applications, stating date of birth and qualifications with dates, accompanied by copies of 3 testimonials, should reach the undersigned not later than 6th October, 1956.

THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

LONDON CHEST HOSPITAL. Hospitals for Diseases of THE CHEST. A vacancy occurs 1st January, 1957, for REGISTRAR in Clinical Pathology (Registrar grade). The appointment (non-resident) is a whole-time one and will be for 1 year in the first instance.

Applications, stating date of birth, qualifications with dates, and previous experience, together with copies of 3 testimonials, should reach the undersigned not later than 15th October, 1956,

THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

LONDON CHEST HOSPITAL. Hospitals for Diseases of THE CHEST. Applications are invited for the post of MEDICAL REGISTRAR. The appointment is for 1 year in the first instance and is non-resident. Duties include outpatients and refill clinic and attendance at the Country Branch, near Letchworth.

Applications, stating date of birth, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should reach the undersigned not later than 15th October, 1956.

THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

LONDON HOSPITAL, Whitechapel, E.1. Applications are invited for the post of SENIOR HOUSE OFFICER to the Receiving Room, becoming vacant on 1st December. The appointment will be for 6 months only and in view of the nature of the duties, preference will be given to applicants who have held a previous appointment at The London Hospital.

Applications (6 copies), together with 6 copies of 3 recent testimonials, should be received by the undersigned by 3rd October, 1956. H. BRIERLEY, House Governor.

LONDON HOSPITAL, Whitechapel, E.1. Applications are invited for the post of SENIOR HOUSE OFFICER to Medical Outpatients Department. The post becomes vacant on 1st December, and will be for 6 months in the first instance. Preference will be given to those trained at The London Hospital.

Applications (6 copies), together with 6 copies of 3 recent testimonials, should be received by the undersigned by 3rd October, 1956. H. BRIERLEY, House Governor.

MARLBOROUGH DAY HOSPITAL, 38, Marlborough-place, N.W.8. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. PSYCHIATRIC REGISTRAR for 3 sessions per week. Clinic may be visited by direct appointment.

Application forms from, and returnable to, Group Secretary, Central Middlesex Group Hospital Management Committee, Acton-lane, N.W.10, by 2nd October, 1956.

MIDDLESEX HOSPITAL, W.1. Applications invited for non-resident posts of REGISTRAR and of SENIOR HOUSE OFFICER in the Department of Physical Medicine and Rheumatism.

Rules and application forms obtainable from Deputy Superintendent should be returned, naming 2 referees, by 6th October.

MILDMAY MISSION HOSPITAL, Austin-street, Bethnal Green, London, E.2. Applications are invited from registered medical practitioners for the post of RESIDENT SENIOR HOUSE OFFICER. Recognised for the F.R.C.S. Vacant 1st November, 1956. The appointment is for 1 year. Salary £745 p.a., less residential charges. Candidates should be in full sympathy with the evangelistic aims of the Hospital.

Applications and references to be addressed to the Medical Superintendent.

MILE END HOSPITAL, Bancroft-road, London, E.1. (484 Beds.) HOUSE PHYSICIAN (pre- or post-registration). Post vacant 18th October, 1956.

Application forms, obtainable from Physician-Superintendent, should be returned by 28th September, 1956, with copies of not more than 3 testimonials.

NELSON HOSPITAL, Kingston-road, Merton, S.W.20. RESIDENT ANÆSTHETIST (Senior House Officer grade).

Applications, stating age, experience and qualifications, with copies of testimonials and the name of 1 referee, should be sent to the Group Secretary, St. Helier Hospital, Carshalton, Surrey.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

GERIATRIC REGISTRAR (resident), St. Matthew's Hospital, N.1.

GENERAL SURGICAL AND ORTHOPÆDIC REGISTRAR (resident), Metropolitan Hospital, E.8. Candidates must possess F.R.C.S.

SURGICAL REGISTRAR (resident), Victoria Hospital, Romford, Essex.

SURGICAL REGISTRAR (resident or non-resident), Poplar Hospital, E.14. Recognised for F.R.C.S.

ANÆSTHETIC REGISTRAR (resident or non-resident near Hospital), St. Leonard's Hospital, N.1. Recognised for D.A.

ANÆSTHETIC REGISTRAR (resident or non-resident near Hospital), St. Andrew's Hospital, Billericay, Essex. Recognised for D.A. and F.F.A.R.C.S.

OBSTETRIC REGISTRAR (resident), Thorpe Coombe Maternity Hospital, Forest-road, E.17. Recognised for M.R.C.O.G.

REGISTRAR in Obstetrics and Gynæcology (non-resident), Prince of Wales's General Hospital, Tottenham, N.15, and Bearstead Memorial Hospital. Recognised at The Prince of Wales's General Hospital for D.Obst.R.C.O.G. and M.R.C.O.G.

REGISTRAR in Pathology (resident), St. Ann's General Hospital, Tottenham, N.15.

Appointments subject to review after 1 year.

Application forms from Secretary, 11A, Portland-place, W.1, to be returned by 6th October, 1956.

NORTH MIDDLESEX HOSPITAL, Edmonton, N.18. HOUSE SURGEON (resident) required, for 1st November for 6 months. General surgery and some E.N.T. surgery. Post recognised for F.R.C.S.

Applications (in own handwriting), stating age, nationality, qualifications, experience, with copies of recent testimonials, to Secretary of Hospital, by 2nd October.

NORTH MIDDLESEX HOSPITAL, Edmonton, N.18. 2 OBSTETRIC AND GYNÆCOLOGICAL HOUSE SURGEONS (resident) required for 1st November, 1956.

(*a*) Registered medical practitioner.

(*b*) Pre-registration candidate (second post).

Both posts recognised by R.C.O.G. for Diploma, and as a combined post for Membership. Candidates must have held house appointments in either medicine or surgery. Large Obstetric and Gynæcological Department.

Applications (in own handwriting), stating age, nationality qualifications, experience, with copies of recent testimonials, to Secretary of Hospital, by 2nd October.

PADDINGTON GREEN CHILDREN'S HOSPITAL. (ST. MARY'S HOSPITAL, W.2.) Applications are invited for the post of CASUALTY OFFICER (post-registration appointment), non-resident, House Officer grade, tenable for 6 months as from 1st November, 1956.

Applications, stating age, nationality, qualifications with dates, and experience, with copies of 3 recent testimonials, should reach the Secretary not later than 29th September, 1956.

QUEEN ELIZABETH HOSPITAL FOR CHILDREN MANAGEMENT COMMITTEE, Hackney-road, E.2, Shadwell, E.1, and BANSTEAD WOOD, SURREY. RESIDENT MEDICAL OFFICER (Male or Female), graded Senior House Officer at Banstead. Applications are invited for the above appointment vacant now. Candidates must have had experience in the treatment of sick children. The appointment will be for 6 months or 1 year.

Application forms may be obtained from the Secretary at Hackney-road, and should be returned, with copies of not more than 3 testimonials, as soon as possible.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, London, E.15. JUNIOR CASUALTY OFFICER (House Officer third post) required for 6 months commencing as soon as possible.

Applications, with copies of recent testimonials, to Hospital Secretary by 27th September, 1956.

ROYAL FREE HOSPITAL. Applications are invited for the post of REGISTRAR to the X-ray Department of the Royal Free Hospital. The post is non-resident, for 1 year in the first instance. Duties to commence 1st November, 1956. Candidates should be registered medical practitioners of not more than 10 years standing and should hold the D.M.R.(D.).

Formal applications, giving details of experience, &c., together with 3 testimonials, should be sent to the Secretary, Royal Free Hospital, Gray's Inn-road, W.C.1, not later than 30th September, 1956.

ROYAL MARSDEN HOSPITAL, Fulham-road, London, S.W.3. Applications are invited from registered medical practitioners for the post of HOUSE SURGEON (resident) to commence duty on 10th November, 1956. Salary £525 p.a. The post is tenable for 6 months.

Forms of application are obtainable from the House Governor, to whom applications, together with copies of 3 recent testimonials, should be sent not later than 8th October, 1956.

ROYAL NATIONAL THROAT, NOSE AND EAR HOS-PITAL, Gray's Inn-road, W.C.1, and Golden-square, W.1. In association with The Institute of Laryngology and Otology. Applications are invited for a post of REGISTRAR or alternatively SENIOR HOUSE OFFICER. A higher surgical qualification is required for the former grading and at least the Primary F.R.C.S. for the latter. Considerable clinical experience in general surgery and in this specialty is required for either post. The appointment will be in accordance with the terms and conditions of service for the appropriate grade in the National Health Service.

Applications, giving full information and the names of 2 referees, should be sent to the House Governor by 1st October.

ROYAL NORTHERN HOSPITAL, Holloway, N.7. (279 Beds.) NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. MEDICAL REGISTRAR (second) required at the above Hospital. Candidates may visit the Hospital by direct appointment.

Application forms obtainable from, and returnable to, the Secretary, Royal Northern Hospital, N.7, by 2nd October, 1956.

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN, Clapham Common, S.W.4. Applications are invited for the post of SENIOR RESIDENT MEDICAL OFFICER (Woman), Senior House Officer grade. Appointment for 6 months; renewable. Duties include care of children's ward; medical beds; E.N.T. and administration. Offers suitable experience to those intending to enter General Practice. Vacant 1st November, 1956.

Application forms from the Secretary.

ST. ANDREW'S HOSPITAL, Bow, E.3. Applications are invited for the appointment of HOUSE SURGEON (orthopædic, E.N.T., and emergency surgery). Recognised pre-registration post. Vacant on 21st October, 1956. Post is tenable for 6 months.

Applications, stating age and qualifications, with copy of at least 1 testimonial, should be sent immediately to the Hospital Secretary, St. Andrew's Hospital, Bow, E.3.

ST. ANDREW'S HOSPITAL, Bow, E.3. Applications are invited for the appointment of HOUSE PHYSICIAN. Recognised pre-registration post. Vacant on 10th October, 1956, and tenable for 6 months.

Applications, stating age and qualifications, with copy of at least 1 testimonial, should be sent immediately to the Hospital Secretary, St. Andrew's Hospital, Bow, E.3.

ST. JAMES' HOSPITAL, Balham, S.W.12. Senior House OFFICER to Medical Unit. Duties include staff examinations. Post vacant end of October.

Applications, stating age, qualifications, experience, and names of 2 referees, to Group Secretary, Wandsworth Hospital Group, at above address by 3rd October. (42754.)

ST. THOMAS'S HOSPITAL, London, S.E.1. Medical OFFICER to the Department of Venereal Diseases for a period of 1 year in the first instance, to carry out 8 half-day sessions per week. £175 p.a. per weekly session.

Applications, naming 2 referees, to the Clerk of the Governors by 3rd October, 1956.

ST. STEPHEN'S HOSPITAL, Chelsea, S.W.10. South WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SURGICAL REGISTRAR (whole-time), non-resident, vacancy November, 1956. Post recognised for F.R.C.S.

Application forms obtained from and returned (within 14 days) to Group Secretary, St. Luke's Hospital, Sydney-street, S.W.3. (Please enclose foolscap stamped addressed envelope.)

ST. STEPHEN'S HOSPITAL, Chelsea, S.W.10. South WEST METROPOLITAN REGIONAL HOSPITAL BOARD. MEDICAL REGISTRAR to Rheumatism Unit. Non-resident. Vacancy 16th November, 1956. Post offers wide clinical and research experience both in the rheumatic diseases and general medicine. Higher qualifications in medicine desirable but not essential.

Application forms from Group Secretary, St. Luke's Hospital, Chelsea, S.W.3, to be returned within 14 days (enclose foolscap stamped addressed envelope).

ST. MARK'S HOSPITAL, City-road, London, E.C.1. Applications invited from Senior Registrars who have completed their training, or from Registrars who have completed their appointments, for 2 posts of RESIDENT SURGICAL OFFICER. Part of time non-resident by arrangement. Salary at the rate of £1400 or £965 respectively. Appointments tenable for 6 months from 1st December or 1st January with possibility further extension 6 months.

Applications, stating age, qualifications, experience, names of 2 referees, to Secretary, Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, Ducane-road, London, W.12, by 6th October.

ST. MARY'S HOSPITAL, Paddington, W.2. Applications are invited for the post of Part-time REGISTRAR to the Psychiatric Department (5 notional half-days per week). Previous experience in psychiatry is necessary; preference will be given to candidates holding the D.P.M. The appointment will be for a first period of 12 months as from a date to be arranged; remuneration at Registrar rates.

Applications, stating nationality, date of birth, permanent address, qualifications, with dates, details and National Health Service gradings of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 10th October, 1956.

ST. MARY'S HOSPITAL, Paddington, W.2. Applications are invited from suitably qualified Male candidates for the post of Whole-time REGISTRAR in the Venereal Diseases Department. The appointment is for a first period of 12 months as from a date to be arranged, the holder being eligible for re-election.

Applications, stating nationality, date of birth, qualifications, details of experience, together with dates and National Health Service gradings of previous and present appointments and names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 8th October, 1956.

ST. CLEMENT'S HOSPITAL, E.3. Bow Group Hospital MANAGEMENT COMMITTEE. HOUSE PHYSICIAN (not pre-registration) for general medical wards.

Applications, stating age, qualifications, and experience, together with the names and addresses of 2 referees, to be sent to the Hospital Secretary, St. Clement's Hospital, 2a, Bow-road, London, E.3.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy on 22nd November, 1956, for a RESIDENT ANÆSTHETIST (Registrar grade).

Full particulars, with form of application, which must be returned not later than Monday, 15th October, 1956, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There is a vacancy for a NON-RESIDENT SURGICAL OUTPATIENT ASSISTANT (grade: Senior Registrar), attending on Saturday mornings.

Full particulars and form of application, which must be returned not later than 22nd October, 1956, are obtainable from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

UNIVERSITY COLLEGE HOSPITAL, Gower-street, W.C.1. Applications are invited for the appointment of REGISTRAR in the Department of Physical Medicine for 1 year in the first instance.

Applications, with names of 2 referees, to Administrator and Secretary by 6th October, 1956.

WESTMINSTER HOSPITAL, St. John's Gardens, S.W.1. Applications are invited for the post of RESIDENT MEDICAL OFFICER (Female) at Parkwood Auxiliary Hospital, Swanley, Kent, for 1 year in the first instance and renewable. Graded as Junior Hospital Medical Officer. A deduction of £170 p.a. will be made from the salary for board-residence. The post offers opportunity for study.

Applications (4 copies), with names of 2 referees, to House Governor.

WESTMINSTER HOSPITAL, St. John's Gardens, S.W.1. Applications invited for vacant post of SENIOR REGISTRAR, to Radiotherapy Department for 1 year in first instance. Preference given to candidates holding M.R.C.P., F.R.C.S., or other higher qualification. Successful applicant must take D.M.R.T., during tenure if not already held.

Applications (9 copies), with names of 2 referees, to House Governor by 6th October.

WESTMINSTER HOSPITAL, St. John's Gardens, S.W.1. Applications invited for post of REGISTRAR to Radiotherapy Department for 1 year in first instance from 15th October, 1956. Preference gien to candidates holding F.R.C.S. or M.R.C.P. Experience of general medicine or surgery in Registrar grade an advantage. Knowledge of radiotherapy not essential.

Applications (7 copies), with names of 2 referees, to House Governor by 6th October.

WILLESDEN GENERAL HOSPITAL, Harlesden-road, N.W.10. Locum RESIDENT CASUALTY OFFICER (Senior House Officer) required 12th–26th October.

Apply Hospital Secretary.

WOOLWICH GROUP HOSPITAL MANAGEMENT COMMITTEE.

OBSTETRICAL HOUSE OFFICER, British Hospital for Mothers and Babies, Samuel-street, Woolwich. Recognised for D.Obst.R.C.O.G. and M.R.C.O.G. Approved for Pre-registration Service. Vacant 1st November.

HOUSE SURGEON (gynæcology and obstetrics), Memorial Hospital, Shooters Hill, Woolwich. Recognised for M.R.C.O.G. (6 months gynæcology). Small Obstetric Unit providing good experience. Vacant early November.

Applications to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ABERYSTWYTH GENERAL HOSPITAL. Applications are invited for the following posts:—

HOUSE PHYSICIAN.

Locum HOUSE SURGEON.

Applications to the Group Secretary, Mid Wales Hospital Management Committee, 31, North-parade, Aberystwyth, Cards.

ASHFORD HOSPITAL, Ashford, Middlesex. Staines GROUP HOSPITAL MANAGEMENT COMMITTEE. Required, RESIDENT HOUSE SURGEON (Male) for Traumatic and Orthopædic Unit on 1st November, 1956. 6 months appointment suitable for pre-registration candidates.

Applications, stating age, qualifications and experience with copies of up to 3 recent testimonials, to Medical Director of Hospital.

ASHFORD HOSPITAL, Ashford, Middlesex. (560 Beds.) STAINES GROUP HOSPITAL MANAGEMENT COMMITTEE. Required, RESIDENT HOUSE OFFICER (Male) for general surgical and medical duties. 6 months appointment, not suitable for pre-registration candidates.

Applications, stating age, qualifications, and experience, with copies of up to 3 recent testimonials, to Medical Director of Hospital.

ASHFORD HOSPITAL, Ashford, Kent. Applications are invited for the appointment of SENIOR HOUSE SURGEON at the above Hospital. The appointment will be tenable for a year. Salary £745 a year, less a deduction of £150 a year for residential emoluments.

Applications, stating age, qualifications and the names and addresses of 2 referees, should be made to the Group Secretary, "Ash-Eton," Radnor Park West, Folkestone.

ALTON, HAMPSHIRE. LORD MAYOR TRELOAR ORTHOPÆDIC HOSPITAL. (340 Beds—Adults and Children.) SENIOR ORTHOPÆDIC REGISTRAR required, whole-time, resident. Post available for 1 year and is approved by the British Postgraduate Medical Federation to give Senior Orthopædic Registrars an opportunity of spending 1 year in an active Orthopædic Hospital with many long-stay orthopædic patients. Attendance necessary at peripheral clinics. Quarters for a single man: unfurnished 3-bedroom house for married man. Canvassing disqualifies but visit to Hospital (by appointment) welcomed.

Application form from Secretary.

BEDFORD GENERAL HOSPITAL. (439 Beds.) House SURGEON required (mainly orthopædic). Pre- or post-registration; recognised for F.R.C.S. Vacant mid-October. Post offers exceptional opportunities for general experience in busy acute surgical units.

Inquiries and applications, with copies of 2 recent testimonials, to Group Secretary, 3, Kimbolton-road, Bedford.

BEDFORD GENERAL HOSPITAL. (439 Beds.) North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. GENERAL SURGICAL REGISTRAR (resident) required at above Hospital which may be visited by direct appointment. Post vacant October.

Application forms obtainable from, and returnable to, Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford, as soon as possible.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. (229 Beds.) HOUSE PHYSICIAN (House Officer or Senior House Officer grading according to experience), vacant end of September. Pre-registration post but fully qualified practitioners may apply.

Applications to Group Secretary.

BISHOP'S STORTFORD. HERTS AND ESSEX GENERAL HOSPITAL. (Formerly Haymeads Hospital.) Applications are invited from registered medical practitioners for the appointment of a Whole-time Temporary SURGICAL REGISTRAR to commence 27th September, 1956, for 1 month in first instance followed by engagement on a week-by-week basis.

Applications, giving full details, together with copies of recent testimonials, or the names of referees, to the Group Secretary, Hertford Hospital Management Committee, County Hospital, Hertford, Herts.

BISHOP AUCKLAND. GENERAL HOSPITAL. (300 Beds.) SOUTH WEST DURHAM HOSPITAL MANAGEMENT COMMITTEE. REGISTRAR ORTHOPÆDIC SURGEON (whole-time) at above Hospital. 51-Bed Orthopædic Unit. Married or single accommodation available.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Newcastle Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6.

BIRMINGHAM, 18. DUDLEY ROAD HOSPITAL. (780 Beds.) HOUSE SURGEON required. Recognised for pre-registration and F.R.C.S. Unit of approximately 85 adult and children's general surgical beds under control of 2 Consultant Surgeons.

Detailed applications, with copies of 3 recent testimonials, to Group Secretary.

BIRMINGHAM. THE UNITED BIRMINGHAM HOS-PITALS. THE CHILDREN'S HOSPITAL, Ladywood-road, BIRMINGHAM, 16. Applications are invited for the appointment of RESIDENT SENIOR HOUSE OFFICER to work in the Clinical Pathological Department, vacant 8th November, 1956, for 1 year. Applicants should have held resident appointments in a children's hospital or a children's department of a general hospital.

Forms of application may be obtained from the House Governor and should be returned by 6th October, 1956.

G. A. PHALP, Secretary to the Board of Governors.

BIRMINGHAM. UNITED BIRMINGHAM HOSPITALS. BIRMINGHAM AND MIDLAND HOSPITAL FOR WOMEN, Showell Green-lane, SPARKHILL, BIRMINGHAM, 11. Applications are invited from registered medical practitioners for the post of RESIDENT GYNÆCOLOGICAL HOUSE SURGEON for duty with the Professorial Unit from 1st December, 1956. The appointment is recognised for the M.R.C.O.G. and D.Obst.R.C.O.G.

Application forms, obtainable from the House Governor at the above address, to be returned not later than 6th October, 1956. G. A. PHALP, Secretary.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Whole-time SENIOR REGISTRAR in Ophthalmology. Duties at North Staffordshire Royal Infirmary (455 Beds). Higher qualification/wide experience specialty essential. Resident or non-resident (3 miles radius of Hospital). Successful candidate may subsequently be required to spend not more than 2 years in a selected hospital of the United Birmingham Hospitals in accordance with the arrangements for the interchange of Registrars agreed between the 2 Boards.

Applications (15 copies), naming 3 referees, to Secretary, Regional Hospital Board, 10, Augustus-road, Birmingham, 15, before 8th October, 1956.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

(1) **Birmingham No. 6 Group (Mental B), Hollymoor Hospital, Northfield, Birmingham, 31** (745 Beds)

REGISTRAR (resident/non-resident). Experience in investigation, diagnosis, and treatment all psychiatric illness. D.P.M. course, Birmingham University.

(2) **Stoke-on-Trent Group, Princes-road, Stoke-on-Trent**

REGISTRAR (pathology), resident, for City General Hospital (845 Beds). Laboratory recognised for Dip. Path. Excellent experience in specialty available. Library facilities.

(3) **Walsall Group, Walsall General Hospital, Walsall**

REGISTRAR (general medicine), resident. Group appointment. Duties mainly at Manor Hospital. Experience specialty essential.

Application forms from Group Secretaries, to be returned by 1st October, 1956.

BIRMINGHAM ACCIDENT HOSPITAL, Bath-row, BIRMINGHAM, 15. (215 Beds and 8 House Surgeons.) HOUSE SURGEON (resident) vacant end September. Recognised for purpose of Casualty by R.C.S. (Eng.). Teaching programme by Consultant Staff. Appointment for 6 months, some of which may be spent, at applicant's request, in 42-Bedded Medical Research Council's Burns Unit.

Applications, naming 2 referees, to Administrator.

BIRMINGHAM, 13. SORRENTO MATERNITY HOS-PITAL, Wake Green-road. (106 Beds including 24 premature baby cots.) OBSTETRIC HOUSE SURGEON. Recognised for D.Obst.R.C.O.G. Hospital affiliated to Birmingham Medical School for training of students. Vacant 1st November.

Apply Obstetrician by 26th September.

BLACKBURN AND DISTRICT HOSPITAL MANAGE-MENT COMMITTEE. HOUSE SURGEONS (3) required for the following hospitals:—

Royal Infirmary, Blackburn (262 general beds)—28th October and 1st November.

Queen's Park Hospital, Blackburn (640 mainly general beds)—1st November.

Applications to Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn, Lancs.

BLACKBURN AND DISTRICT HOSPITAL MANAGE-MENT COMMITTEE. REGISTRAR (anæsthetics) required. Resident post. Married accommodation available if desired. Duties mainly at Blackburn Royal Infirmary with sessions at Victoria Hospital, Accrington, and Queen's Park Hospital, Blackburn, as arranged by Consultant-in-charge. Post recognised for D.A. and F.F.A.R.C.S.

Application forms available from Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn, Lancs.

BLACKBURN AND DISTRICT HOSPITAL MANAGE-MENT COMMITTEE. Locum REGISTRAR (anæsthetics) required from 7th October.

Apply to Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn, Lancs.

BLACKPOOL. VICTORIA HOSPITAL. (348 Beds.) Applications are invited for the post of RESIDENT HOUSE OFFICER (gynæcology and obstetrics) which is recognised for the M.R.C.O.G. and for pre-registration purposes. Post vacant 1st November, 1956. This is a busy general hospital with a large Outpatient Department and the post offers excellent opportunities for experience under Consultant Gynæcologists and Obstetricians.

Applications, with names and addresses of referees, to the Hospital Secretary.

BOLTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE.

Bolton District General Hospital (604 Beds)

RESIDENT SENIOR HOUSE OFFICER for general surgical duties. Vacant 31st October, tenable for 12 months and recognised for F.R.C.S.

The Royal Infirmary, Bolton (237 Beds)

RESIDENT SENIOR HOUSE OFFICER in Orthopædic Surgery. Vacant 29th October, tenable for 12 months and recognised for F.R.C.S.

Applications, stating age, nationality, qualifications, experience, and the names of 2 referees, to Group Secretary, The Royal Infirmary, Bolton.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, WESTBOURNE, HANTS. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT SENIOR HOUSE OFFICER for E.N.T. and Ophthalmic duties. The appointment which becomes vacant on 22nd September, 1956, is recognised for the D.O. and D.L.O. Diplomas. In addition to duties at the above Hospital, the successful candidate will be required to assist in E.N.T. outpatient clinics at the Royal Victoria Hospital, Shelley-road, Bournemouth, and Poole General Hospital, Poole.

Applications to the Hospital Secretary, Royal Victoria Hospital, Shelley-road, Bournemouth.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (312 Beds.)

2 HOUSE SURGEONS required mid- and end-October.

2 HOUSE PHYSICIANS required mid-October and mid-November.

All posts recognised for pre-registration and F.R.C.S.

Applications, stating usual particulars, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRISTOL. SOUTHMEAD GENERAL HOSPITAL GROUP MANAGEMENT COMMITTEE. Required immediately at Southmead Hospital (571 Beds, including 133 maternity) RESIDENT SENIOR HOUSE OFFICER (pathology). General experience in clinical pathology, including blood transfusion duties. (There is a possibility of a further years appointment with basic training in morbid anatomy.)

Applications to be submitted to the Group Secretary, Southmead Hospital, Bristol.

BRISTOL. THE BOARD OF GOVERNORS OF THE UNITED BRISTOL HOSPITALS AND THE SOUTH-WESTERN REGIONAL HOSPITAL BOARD. Applications are invited by the above Boards for the joint appointment of SENIOR REGISTRAR in Psychiatry to the Plymouth Clinical Area based on Moorhaven Hospital, Ivybridge, South Devon. The appointment will be held for 1 year in the first instance but may be renewed thereafter on an annual basis. A flat is available suitable for a married man. A comprehensive mental health service is in operation, and experience can be gained in all branches of inpatient and outpatient work (including neurology, mental deficiency and child guidance). The outpatient service is based on the South Devon and East Cornwall Hospital, Plymouth, and the Plymouth Child Guidance Clinic. The 1955 Annual Report which gives full particulars of the service can be obtained from the Physician-Superintendent, Moorhaven Hospital.

Applications, stating date of birth, qualifications and experience together with the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 29th September, 1956.

BRISTOL. THE BOARD OF GOVERNORS OF THE UNITED BRISTOL HOSPITALS AND THE SOUTH-WESTERN REGIONAL HOSPITAL BOARD. Applications are invited by the above Boards for the joint appointment of REGISTRAR in Pædiatrics. This post becomes vacant on 6th December, 1956. The appointment, which is resident, will be held for 1 year in the first instance and be renewable for a further year. The successful candidate will be appointed to work for the first year at Southmead Hospital, Bristol, which is associated with the University Departments of Child Health and Obstetrics. The post offers excellent experience in general pædiatrics, neonatal pædiatrics, and care of the premature baby.

Applications, stating date of birth, qualifications and experience, together with the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 29th September, 1956.

BROXBURN, WEST LOTHIAN. BANGOUR GENERAL HOSPITAL. E.N.T. UNIT. Applications are invited for the post of REGISTRAR in the E.N.T. Unit at Bangour General Hospital, Broxburn (15 miles from Edinburgh), which carries certain minimal duties at the Royal Infirmary, Edinburgh. The Unit comprises 40 Beds and also undertakes oral dental surgery. Salary and conditions of service will be in accordance with the regulations.

Applications, giving age, qualifications and particulars of previous experience, should be lodged with the Group Secretary and Treasurer, Board of Management, Bangour General Hospital, Broxburn, West Lothian.

BROXBURN, WEST LOTHIAN. BANGOUR GENERAL HOSPITAL. (15 miles from Edinburgh.) Applications are invited for the appointment of SENIOR HOUSE OFFICER in the Ophthalmic Unit (32 Beds) at Bangour General Hospital, Broxburn, which is associated with the Ophthalmic Unit of the Royal Infirmary, Edinburgh. Salary and conditions of service will be in accordance with the regulations.

Applications, giving age, qualifications and particulars of previous experience, should be lodged with the Group Secretary and Treasurer, Board of Management, Bangour General Hospital, Broxburn, West Lothian.

BURTON UPON TRENT GENERAL HOSPITAL. Junior HOSPITAL MEDICAL OFFICER (orthopædic) required at the above Hospital. Duties include supervision of Casualty House Officer.

Applications to Group Secretary.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. ROSSENDALE GENERAL HOSPITAL, RAWTENSTALL. Applications are invited for the post of SENIOR HOUSE OFFICER in Medicine at the above Hospital.

Apply, stating age, experience, qualifications, and names of 2 referees, to H. WILKINSON, Group Secretary.

Bury General Hospital, Bury, Lancs.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) The post of GENERAL SURGICAL AND ORTHOPÆDIC HOUSE SURGEON, which is recognised for the F.R.C.S. Diploma, is now vacant. National Health Service salary and conditions.

Applications, together with 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CARLISLE. GARLANDS HOSPITAL. (1060 Beds.) GARLANDS HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER at the above Mental Hospital. Salary £745 p.a. Flat is available for which a deduction will be made. Appointment is subject to the National Health Service superannuation regulations and to the conditions and terms of service laid down by the Minister of Health.

Applications, stating age, qualifications and experience, and the names of 2 referees, should be sent to the Medical Superintendent as soon as possible.

COLCHESTER. ESSEX COUNTY HOSPITAL. (188 Beds.) Applications are invited for :—

SENIOR HOUSE OFFICER (casualty and E.N.T.).

SENIOR HOUSE OFFICER (casualty and radiotherapy).

Posts recognised for F.R.C.S. ; tenable for 6 months or 1 year.

Applications, with copies of 3 testimonials, to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

CARDIFF (near). PRINCE OF WALES ORTHOPÆDIC HOSPITAL, RHYDLAFAR, near CARDIFF. SENIOR HOUSE OFFICER required. Regional Orthopædic Centre for South Wales area of 220 Beds increasing to 290 and branch of 70 Beds. Outpatient clinic in Cardiff. Single accommodation at hospital at Rhydlafar.

Form of application from Group Secretary, 4 Cathedral-road, Cardiff.

CARDIFF (near). CAERPHILLY DISTRICT MINERS HOSPITAL. (226 general beds.) SENIOR HOUSE OFFICER (general surgery).

Apply to Group Secretary, Rhymney and Sirhowy Valleys Hospital Management Committee, Central Offices, Caerphilly-road, Ystrad Mynach, Hengoed, Glam.

CHELMSFORD. ST. JOHN'S HOSPITAL. Locum RESIDENT ANÆSTHETIST required to commence 27th September for approximately 6 weeks.

Applications to the Group Secretary, Chelmsford Hospital Management Committee, Chelmsford and Essex Hospital, London-road, Chelmsford, Essex.

CHELTENHAM MATERNITY HOSPITAL. Cheltenham GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of RESIDENT OBSTETRIC OFFICER. The Hospital, which is recognised for the purpose of training for the D.Obst.R.C.O.G., has 50 Beds and deals with the majority of abnormal midwifery cases in North East Gloucestershire. The appointment is for a period of 6 months and the salary will be £425, £475, or £525 p.a., less £125 in respect of residential emoluments. The appointment will be vacant on 20th October, 1956.

Applications, stating age, qualifications, and experience, and accompanied by copies of 3 recent testimonials, should be sent to the Secretary, Cheltenham Group Hospital Management Committee, General Hospital, Cheltenham.

CHESTER ROYAL INFIRMARY. Applications are invited for the post of RESIDENT CASUALTY OFFICER (Junior Hospital Medical Officer). The post is recognised for the F.R.C.S.

Applications, giving full details, together with the names and addresses of 2 referees, should be forwarded to the Group Secretary, Chester and District Hospital Management Committee, 5, King's-buildings, Chester.

CLACTON AND DISTRICT HOSPITAL, Clacton-on-Sea. (58 Beds.) Applications invited for post of SENIOR HOUSE OFFICER (Resident Surgical Officer). Post tenable for 1 year.

Applications, with copies of 3 testimonials, to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

CROMER AND DISTRICT HOSPITAL, Norfolk. Applications are invited for the post of RESIDENT MEDICAL OFFICER (Senior House Officer status). Post vacant October, 1956, at a salary of £745 p.a., in accordance with conditions of service issued by the Ministry of Health. This is a busy general hospital of 50 Beds which has a pre-convalescent annexe of 64 Beds and an Outpatient Department where Consultants in all the major specialties hold regular sessions. The appointment thus offers practical experience of an all-round kind particularly useful to those contemplating entry into general practice. Residential accommodation available or furnished flat for married man.

Applications, stating age, qualifications, experience, sex, and the names of 2 referees, should be addressed to the Secretary, Cromer Area Hospital Management Committee, Cliff-avenue, Cromer.

CROWTHORNE, BERKSHIRE. BROADMOOR INSTITUTION. (920 Beds for persons of unsound mind of criminal tendencies.) SENIOR REGISTRAR. House or quarters available.

Applications, naming 3 referees, to Medical Superintendent by 13th October, 1956. Candidates may visit Hospital by appointment.

CROYDON GENERAL HOSPITAL. (200 Beds.) Casualty OFFICER (Senior House Officer—resident). Post vacant 22nd October, 1956. Recognised for Final F.R.C.S. examination. There is a Registrar in charge of Department.

Application forms obtainable from GEORGE A. PAINES, Group Secretary, Croydon Hospital Management Committee, General Hospital, Croydon.

DERBY. DERBYSHIRE ROYAL INFIRMARY. (416 Beds. Derby Group recognised for training for F.F.A.R.C.S. and D.A.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (anæsthetics) required. Duties will include attendances at other hospitals in the Group. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 1st October, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

DEWSBURY, YORKSHIRE. THE GENERAL HOSPITAL. Applications are invited for the pre-registration post of HOUSE OFFICER (general surgery) which is available immediately.

Applications, giving full details and the names of 3 referees, should be sent to the Administrative Officer at the Hospital.

DUDLEY, STOURBRIDGE AND DISTRICT HOSPITAL GROUP, BIRMINGHAM REGION.

The Guest Hospital, Dudley (154 Beds)

SENIOR HOUSE OFFICER (casualty). Post now vacant.
SENIOR HOUSE OFFICER (anæsthetics). Post now vacant.
SENIOR HOUSE OFFICER (surgical). Post now vacant.

Wordsley Hospital, near Stourbridge (478 Beds)

SENIOR HOUSE OFFICER (surgical). Post vacant October, 1956.

Apply, Group Secretary, Guest Hospital, Dudley.

EAST GRINSTEAD, SUSSEX. QUEEN VICTORIA HOSPITAL. PLASTIC SURGERY AND JAW INJURIES CENTRE. TUNBRIDGE WELLS GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited for resident appointment of SENIOR HOUSE OFFICER in Anæsthetics, vacant 7th December, 1956. Duties in anæsthesia for both General and Plastic Surgery. Post recognised for the examinations of D.A., and F.F.A.R.C.S.

Apply, stating qualifications, experience and age, and names of 3 referees, by 27th October, 1956, to Group Secretary, Sherwood Park, Pembury-road, Tunbridge Wells.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. REGISTRAR in Psychiatry, East Suffolk Mental Hospitals. St. Clement's Hospital, Ipswich (450 Beds), and St. Audry's Hospital, Melton, near Woodbridge (1100 Beds), and associated General Hospital outpatient clinics. There is a very active Outpatient Department and Electro-encephalographic Department at St. Clement's Hospital. Both hospitals are recognised for the D.P.M. Unfurnished house available. Candidates are invited to visit the hospitals by direct arrangement with Medical Superintendent, St. Audry's Hospital.

REGISTRAR in Psychiatry, St. Andrew's Hospital, Thorpe, Norwich (1250 Beds). Full range of modern psychiatric treatments and a number of associated general hospital outpatient clinics. Married or single quarters available. Appointment for 1 year, renewable for second year. Candidates invited to visit Hospital by direct arrangement with Medical Superintendent.

Applications, stating age, experience, and the names of 3 referees, to the Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 1st October, 1956.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. RESIDENT PÆDIATRIC HOUSE PHYSICIAN for above Hospital. Post vacant 19th November, 1956. 6 months appointment.

Applications, stating age, qualifications, experience, and enclosing copies of up to 3 recent testimonials, to Medical Director of Hospital by 6th October, 1956.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. Temporary REGISTRAR in Orthopædics and General Surgery required for general surgical duties. Non-resident. Appointment vacant 8th October, 1956. Duration 1 month.

Applications, with names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, at Chase Farm Hospital, by 28th September, 1956.

ENFIELD, MIDDLESEX. WAR MEMORIAL HOSPITAL, CHASE SIDE. RESIDENT SENIOR HOUSE OFFICER required for general medical and surgical duties in this Acute General Hospital of 61 Beds. Vacant mid-October. 12 months appointment. Deduction of £150 p.a. for residential emoluments.

Applications, with names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, Chase Farm Hospital, The Ridgeway, Enfield, Middlesex.

EPPING. ST. MARGARET'S HOSPITAL. (480 Beds.) RESIDENT SENIOR HOUSE OFFICER. Post vacant 1st November, 1956. Required for Chest Department and to act as Second Resident Anæsthetist. Good opportunity for experience in modern methods. Previous experience in chest diseases desirable but not essential.

Applications, with references, to reach Group Secretary, Epping Group Hospital Management Committee, "Oak Cottage," The Plain, Epping, Essex, by 28th September.

EPPING. ST. MARGARET'S HOSPITAL. (480 Beds.) RESIDENT SENIOR HOUSE OFFICER (surgery) as Casualty Officer and Orthopædic House Surgeon. Post vacant 1st October, 1956. Recognised training post for F.R.C.S. Busy general hospital with easy access to London. Salary on national scale, less deduction for board, lodging, &c.

Applications, with copies of 2 recent testimonials, to the Group Secretary, Epping Group Hospital Management Committee, "Oak Cottage," The Plain, Epping, Essex.

EPSOM GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for Whole-time REGISTRAR in Chest Medicine to the Epsom and Dorking Chest Clinics. Vacancy 1st December, 1956. Duties will include sessions at 1 or both clinics. Additionally, person appointed will be Registrar at Cheam Sanatorium where there are 53 Beds for the treatment of cases of pulmonary tuberculosis, and will have the day-to-day care of patients under the various Consultants concerned. Successful candidate will be required to live within easy access of Cheam Sanatorium. Applicants may visit Units by arrangement with Consultant Chest Physician.

Application forms may be obtained from Group Secretary, Epsom District Hospital, Dorking-road, Epsom (send stamped addressed foolscap envelope), for completion and return within 14 days.

GLOUCESTER. HORTON ROAD AND CONEY HILL HOSPITALS. (1450 Beds.) Applications invited for the appointment of a JUNIOR HOSPITAL MEDICAL OFFICER. Hospital serves the North Gloucestershire Clinical Area including Gloucester, Cheltenham, Stroud and Forest of Dean. High admission-rate (800). All modern methods of treatment. New units provided for treatment of neurosis and alcoholism. Expanding outpatient services, long-stay annexes, and social clubs. Encouragement and opportunity for study. Salary and conditions Whitley Council. Single accommodation available. Married accommodation a possibility.

Applications, with names of 3 referees, to Physician-Superintendent within 14 days.

HAREFIELD HOSPITAL. REGIONAL THORACIC SURGICAL UNIT. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the post of SURGICAL REGISTRAR to the Harefield Thoracic Surgical Unit which serves the North West Metropolitan Region. In the Hospital there are 90 Beds for non-tuberculous surgical chest conditions and 446 Beds for tuberculosis. The appointment thus affords a wide experience in all aspects of thoracic surgery. Candidates must have had previous surgical experience and preference will be given to candidates with a higher surgical qualification. The appointment will be held in the first instance for 1 year.

Application forms obtainable from, and returnable to, the Secretary, Harefield and Northwood Group Hospital Management Committee, Mount Vernon Hospital, Northwood, Middlesex, by 2nd October, 1956.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) HOUSE SURGEON (pre-registration post), vacant now. National scale of salary.

Apply to Hospital Administrator.

HITCHIN, HERTFORDSHIRE. LISTER HOSPITAL. Applications are invited for the post of RESIDENT HOUSE SURGEON, vacant 16th October, 1956. Recognised as pre-registration post and for F.R.C.S.

Applications, stating age, nationality, qualifications, and experience, together with copies of 3 recent testimonials, to be sent to the Medical Administrator as soon as possible.

HOLT, NORFOLK. KELLING HOSPITAL AND DEPARTMENT OF THORACIC SURGERY. Applications are invited for the appointment of Locum JUNIOR HOSPITAL MEDICAL OFFICER (minimum of 4 months). This Hospital (180 Beds) deals with tuberculous and non-tuberculous chest conditions and offers excellent experience in chest medicine and thoracic surgery.

Applications, stating age, sex, qualifications, nationality, and experience, together with names of 2 referees, to the Group Secretary, Cromer Area Hospital Management Committee, Cliff-avenue, Cromer, Norfolk, who will be pleased to supply any other information concerning the appointment.

HULL, KINGSTON GENERAL HOSPITAL. (419 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT JUNIOR HOUSE SURGEON (pre- or post-registration). Recognised for the F.R.C.S. examinations. Busy acute General Surgical Unit. Vacant 1st October.

Applications, with 2 recent testimonials, to the Hospital Secretary.

ISLEWORTH, MIDDLESEX. WEST MIDDLESEX HOSPITAL. (1147 Beds—General.) NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. PSYCHIATRIC REGISTRAR required at above Hospital. Whole-time. Non-resident. Recognised D.P.M. (England and R.M.P.A.). Candidates should have special interest in psychotherapy. Psycho-analytical training an advantage. Candidates may visit Hospital by direct appointment with Medical Director.

Application forms obtainable from, and returnable to, Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 29th September, 1956.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required for male and female tuberculosis wards at above Hospital, with part-time duties at Ealing Chest Clinic. Full-time, non-resident. Experience in general medicine advisable and in tuberculosis essential. The Hospital and Clinic may be visited by direct appointment.

Application forms obtainable from, and returnable to, Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, Middlesex, by 3rd October, 1956.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. House OFFICER required for Tuberculosis Unit in large general hospital. Postgraduate training facilities.

Applications, stating age, nationality, qualifications, and experience, with copies of up to 3 recent testimonials, to Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 2nd October, 1956.

KETTERING GENERAL HOSPITAL, Kettering. (170 Beds.) Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER in Anæsthetics. Post recognised for D.A.

Applications, giving details of qualifications and experience, and enclosing copies of 3 recent testimonials, to be sent to the Group Secretary, Kettering and District Hospital Management Committee, at the above address.

KINGSTON-ON-THAMES HOSPITAL GROUP MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER in the Group Laboratory. Whole-time non-resident post. Appointment for 6 months, renewable. Wide general experience in all departments.

Applications to the Group Pathologist, Kingston Hospital, Wolverton-avenue, Kingston-on-Thames, within 7 days of the appearance of this advertisement.

LEICESTER. MARKFIELD HOSPITAL. (163 Beds.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR or SENIOR HOUSE OFFICER (chest diseases) required. Duties will include attendance at chest clinics associated with Hospital under supervision of the Consultant. Minor thoracic procedures are carried out and the staff closely associated with the neighbouring major Thoracic Surgical Unit. Remuneration according to status. Appointment for 1 year in the first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 1st October, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

LEICESTER ROYAL INFIRMARY. Applications are invited for 2 posts of SENIOR HOUSE OFFICER (surgical) for a new Casualty Department. Duties will consist of 6 months as Senior House Officer, Casualty, and 6 months as Senior House Officer in General Surgery. The posts are recognised for the F.R.C.S.

Applications, stating age and qualifications, together with copies of recent testimonials, to the Group Secretary, No. 1 Hospital Management Committee, The Leicester Royal Infirmary, immediately.

LEICESTER ROYAL INFIRMARY. Applications are invited for the posts of SENIOR HOUSE OFFICER (pathology) (2) vacant 1st October. The posts are recognised for D.Path. and D.C.P.

Applications, stating age, qualifications, and experience, together with copies of recent testimonials, to the Group Secretary, No. 1 Hospital Management Committee, The Leicester Royal Infirmary, forthwith.

LEICESTER GENERAL HOSPITAL. Locum Senior HOUSE OFFICER required in Obstetrics and Gynæcology for at least 1 month.

Applications, with copies of testimonials, to Secretary as soon as possible.

LEICESTER ISOLATION HOSPITAL AND CHEST UNIT, Groby-road, LEICESTER. (328 Beds.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (chest and infectious diseases) required. Single accommodation available. This Hospital is also a Thoracic Surgical Centre. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 1st October, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

LEEDS REGIONAL HOSPITAL BOARD. Registrar vacancies.

Anæsthetics

Huddersfield Group (approximately 225 Beds in the Surgical Specialties). Non-resident.

General Surgery

Pinderfields General Hospital (70 general surgical beds). Resident—possibility of married accommodation. Recognition of post by the Royal College of Surgeons applied for.

Infectious Diseases

Castle Hill Hospital, Cottingham (167 infectious diseases beds). Resident.

Psychiatry

(i) Clifton Hospital, York (1100 Beds). Resident or non-resident.

(ii) Stanley Royd Hospital, Wakefield (1976 Beds).

If desired facilities for attending Leeds University will be provided if the successful candidates are studying for the D.P.M.

Applications, stating age, qualifications, and details of present and previous appointments with dates, together with the names and addresses of 3 referees, to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 28th September, 1956.

LEEDS. THE UNITED LEEDS HOSPITALS. The GENERAL INFIRMARY AT LEEDS. SENIOR HOUSE OFFICER in E.N.T. Department required for a period of 6 months from 1st November, 1956. The appointment will be renewable for a further period of 6 months. Terms and conditions of service for hospital medical staff apply.

Applications, giving details of age, qualifications, posts held with dates, and with 3 names for reference, should be sent to the Secretary to the Board as soon as possible.

LEEDS. THE UNITED LEEDS HOSPITALS. The GENERAL INFIRMARY AT LEEDS. SENIOR HOUSE OFFICER in Neurosurgery required for a period of 6 months from 1st November, 1956. The appointment will be renewable for a further period of 6 months. Terms and conditions of service for hospital medical staff apply.

Applications, giving details of age, qualifications, posts held with dates, and with 3 names for reference, should be sent to the Secretary to the Board as soon as possible.

LEEDS. THE UNITED LEEDS HOSPITALS. The GENERAL INFIRMARY AT LEEDS. HOUSE OFFICER (Senior or Junior—pre- or post-registration) required for Department of Urology. Post tenable for 6 months from 1st November, 1956. Salary according to grade. Terms and conditions of service for hospital medical staff apply.

Applications, stating age, qualifications, previous posts with dates, and 3 names for reference, to be sent to the Secretary to the Board as soon as possible.

LEEDS. THE UNITED LEEDS HOSPITALS. The GENERAL INFIRMARY AT LEEDS. RESIDENT RADIOTHERAPY OFFICER (Senior House Officer status). The appointment is for a period of 6 months in the first instance, commencing 1st November, 1956. The post affords facilities for training for D.M.R.T. Conditions of service for hospital medical staff apply.

Applications, stating age, qualifications, previous posts with dates, and 3 names for reference, should be sent to the Secretary to the Board as soon as possible.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. ROYAL LIVERPOOL CHILDREN'S HOSPITAL. Applications are invited for a resident post of SENIOR HOUSE OFFICER in Pædiatrics for duty principally in the Cardiological Department for the period to 30th September, 1957.

Apply by 5th October, 1956, on form obtainable from the Secretary, The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. ST. PAUL'S EYE HOSPITAL. Applications are invited for a post of SENIOR HOUSE OFFICER in Ophthalmology for the period to 30th September, 1957.

Apply as soon as possible on form obtainable from the Secretary, The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1.

MANCHESTER. WEST MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. PARK HOSPITAL, DAVYHULME. Applications are invited from suitably qualified and experienced Male or Female candidates for RESIDENT SURGICAL REGISTRAR (Thoracic Unit). This Hospital is a General Hospital of 433 Beds. It carries out by far the major part of the Manchester Region's cardiac and non-tuberculous thoracic surgery, in addition to all other major specialties. The total number of resident medical staff is 20. The successful candidate will be expected to work with each of the 3 Consultant Thoracic Surgeons attached to this unit of 50 Beds (including 10 children's beds).

Application forms from the Secretary.

MANCHESTER. WEST MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. PARK HOSPITAL, DAVYHULME. (General Hospital—433 Beds.) SENIOR HOUSE OFFICER (general surgery) required. Post vacant end-November.

Application forms from Secretary.

MANCHESTER (near). ALTRINCHAM GENERAL HOSPITAL, ANNEXE AND E.N.T. DEPARTMENT. (183 Beds.) NORTH AND MID-CHESHIRE HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (surgical). This appointment affords excellent experience to suitably qualified candidates. Post recognised under F.R.C.S. regulations.

Applications to Group Secretary, North and Mid-Cheshire Hospital Management Committee, The Hospital, Sinderland-road, Altrincham, Cheshire.

MANCHESTER (near). ALTRINCHAM GENERAL HOSPITAL, ANNEXE AND E.N.T. DEPARTMENT. (183 Beds.) SENIOR HOUSE OFFICER (medical). This appointment is in a busy hospital and offers excellent opportunities of practical experience. Post vacant end of September.

Applications, together with 2 recent testimonials, to Group Secretary, North and Mid-Cheshire Hospital Management Committee, The Hospital, Sinderland-road, Altrincham, Cheshire.

MANCHESTER, 20. CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER (radiotherapy) at the above Hospital, commencing in October, 1956. Training will be available from April, 1957, for Diploma in Radiotherapy Course.

Applications, with full details, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20, immediately.

MANCHESTER. CRUMPSALL HOSPITAL. Applications are invited for the post of REGISTRAR in General Surgery (Resident Surgical Officer). Recognised for F.R.C.S. Vacant 6th October, 1956.

Applications, with names of 2 referees, by 1st October, 1956, to Group Secretary, North Manchester Hospital Management Committee, Crumpsall Hospital, Manchester, 8.

MANCHESTER REGIONAL HOSPITAL BOARD. Bury AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for REGISTRAR in Surgery at Bury General Hospital Post recognised for F.R.C.S.

Applications, together with the names of 2 referees, should be sent to H. WILKINSON, Group Secretary.

Bury General Hospital, Bury, Lancs.

MANCHESTER REGIONAL HOSPITAL BOARD. Senior REGISTRAR in Psychiatry with duties in the Salford Group of hospitals (Salford Royal and Hope Hospitals) and at Springfield Mental Hospital, Manchester.

Application forms, obtainable from the Senior Administrative Medical Officer of the Board, Cheetwood-road, Manchester, 8, should be returned by 8th October, 1956.

MANCHESTER, 23. WYTHENSHAWE HOSPITAL. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of CASUALTY OFFICER (Senior House Officer grade) at Wythenshawe Hospital. This post is recognised by the Royal College of Surgeons.

Applications, stating age, qualifications, present post, and names of 2 referees, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20, within 7 days of the appearance of this advertisement.

NORTH GLOUCESTERSHIRE CLINICAL AREA. The BOARD OF GOVERNORS OF THE UNITED BRISTOL HOSPITALS AND THE SOUTH-WESTERN REGIONAL HOSPITAL BOARD. Applications are invited by the above Boards for the joint appointment of REGISTRAR in General Surgery. The appointment will be held for 1 year in the first instance, and be renewable for a further year. The successful candidate will be appointed to work for the first year mainly at Cheltenham General, Eye and Children's Hospital but may be required to undertake duties in other hospitals in the area.

Applications, stating date of birth, qualifications, and experience, together with the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 29th September, 1956.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the whole-time non-resident appointment of REGISTRAR to the Department of Physical Medicine at the Royal Victoria Infirmary. The appointment is for 1 year in the first instance and will be subject to the terms and conditions of service of hospital medical staff in the National Health Service.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.

Royal Victoria Infirmary, Newcastle upon Tyne.

NEWCASTLE REGIONAL HOSPITAL BOARD. North WEST DURHAM HOSPITAL MANAGEMENT COMMITTEE. REGISTRAR PATHOLOGIST (whole-time) resident. Single accommodation available. Appointment commences 1st January, 1957.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Newcastle Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. Regional THORACIC SERVICE. 2 REGISTRAR THORACIC SURGEONS (whole-time) resident, at Regional Thoracic Centre (150 Beds), Shotley Bridge General Hospital. Work almost entirely non-tuberculosis (cardiovascular, œsophageal, and pulmonary) and at associated sanatoria. Applicants must have had good experience in general surgery and a higher qualification or its equivalent. Appointment intended either for a trainee in thoracic surgery or for a general surgeon seeking special experience. Single accommodation available.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Newcastle Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. North-ALLERTON HOSPITAL MANAGEMENT COMMITTEE. REGISTRAR SURGEON (whole-time) resident. Friarage Hospital (340 Beds). Accommodation available. Recognised for F.R.C.S. examination.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Newcastle Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NEWMARKET GENERAL HOSPITAL, Suffolk. Applications are invited for the post, now vacant, of SENIOR HOUSE OFFICER, for orthopædic and casualty duties. The post is resident.

Applications, giving age, nationality and qualifications, together with 3 recent testimonials, should be sent to the Medical Superintendent.

NORTHAMPTON GENERAL HOSPITAL. (482 Beds.) Vacancies 1st October, 1956, for the following :—

HOUSE OFFICER (general surgery); recognised for F.R.C.S.
HOUSE OFFICER (Department of Anæsthetics); recognised for D.A.
HOUSE OFFICER (Pædiatric Department); recognised for D.C.H.
HOUSE OFFICER (Fracture and Orthopædic Department); recognised for F.R.C.S.
HOUSE OFFICER (Casualty Department); recognised for F.R.C.S.
SENIOR HOUSE OFFICER (Casualty Department); recognised for F.R.C.S.
SENIOR HOUSE OFFICER (E.N.T. Department); recognised for F.R.C.S. and D.L.O.
SENIOR HOUSE OFFICER (Department of Pathology).

All posts, except those of Anæsthetic House Officer and the Senior House Officer posts, recognised for pre-registration. Casualty House Officer and Pædiatric House Officer posts recognised for medical pre-registration. All 6 months appointments in first instance.

Applications, enclosing copies of 3 testimonials, as soon as possible, to S. G. HILL, Superintendent.

NORTHAMPTON (near). CREATON SANATORIUM. Applications are invited from suitably qualified medical practitioners for the post of SENIOR HOUSE OFFICER. The Sanatorium has 138 Beds and is for the treatment of both pulmonary and non-pulmonary tuberculosis. There is a new major Thoracic Surgical Unit for tuberculous and non-tuberculous diseases of the chest.

Applications, stating age, experience, and qualifications, together with the names and addresses of 2 referees, should be sent to the Secretary, Northampton and District Hospital Management Committee, General Hospital, Northampton.

NORWICH. ST. ANDREW'S HOSPITAL, Thorpe, NORWICH. Applications are invited from registered medical practitioners (Male or Female) for the appointment of SENIOR HOUSE OFFICER (psychiatric). The Hospital has 1250 Beds, an admission rate of over 600 annually and affords comprehensive experience in psychiatry. The salary and conditions of service will be as laid down by the Ministry for Senior House Officers. Residential accommodation with board available.

Applications, stating age, qualifications and full particulars of experience, together with the names and addresses of 2 referees, to be sent as soon as possible to the Medical Superintendent.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER (casualty) duties to commence immediately. Establishment 3. Recognised for F.R.C.S. Post offers wide experience of casualty work.

Applications, stating age, nationality, qualifications and experience, together with copies of testimonials, to be sent to the Secretary, General Hospital, Nottingham.

NOTTINGHAM. HIGHBURY HOSPITAL. Senior HOUSE OFFICER (surgical) required at the above Hospital. Good opportunity for obtaining experience in all types of general surgery. Duties to commence immediately.

Applications, stating age, qualifications and experience, and nationality, together with copies of testimonials, to be sent to the Group Secretary, General Hospital, Nottingham.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL.

HOUSE SURGEON (pre-registration post), vacant 1st December, 1956. Recognised for the F.R.C.S. Devonport Section.

HOUSE SURGEON (pre-registration post), vacant 1st December, 1956. Recognised for the F.R.C.S. Greenbank Road Section.

Applications, stating age, nationality, qualifications and experience, together with the names and addresses of 3 referees, to be sent to—

ARTHUR R. CASH, Group Secretary, Plymouth,
South Devon and East Cornwall General Hospital Group.
7, Nelson-gardens, Stoke, Plymouth.

PLYMOUTH. MOUNT GOLD HOSPITAL. Senior HOUSE OFFICER for the Orthopædic and Fracture Service centring on Mount Gold Orthopædic, with annexe (122 Beds) and associated Hospitals. Post recognised by R.C.S. Married accommodation available.

Applications, stating age, qualifications with dates, &c., and with copies of 2 recent testimonials, to be forwarded to the Secretary within 14 days of this advertisement appearing.

PONTEFRACT AND CASTLEFORD HOSPITAL MAN-AGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER to Assist Geriatric Physician in the staffing of an active Geriatric Unit at hospitals in this and Wakefield A Hospital Management Committee area. Car essential. Post vacant from 18th October, 1956.

Applications immediately to the Secretary, Great Northern House, Salter-row, Pontefract, Yorkshire, giving the names of 2 referees.

OSWESTRY. THE ROBERT JONES AND AGNES HUNT ORTHOPÆDIC HOSPITAL. SENIOR HOUSE OFFICER (2 vacancies), resident.

Apply Secretary.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE.

(1) **Queen Alexandra Hospital**
SENIOR HOUSE SURGEON (recognised for the F.R.C.S.) (87 surgical beds), vacant now.
(2) **Royal Portsmouth Hospital**
(*a*) SENIOR HOUSE SURGEON (recognised for the F.R.C.S.) (70 surgical beds) vacant now.
(*b*) ANÆSTHETIST (Senior House Officer grade). Recognised for the F.F.A.R.C.S. Vacant 1st October, 1956.

Applications, stating age, experience and qualifications, together with the names of 2 referees, should be forwarded as soon as possible to E. H. HURST.

St. Mary's Hospital, Milton-road, Portsmouth.

PORTSMOUTH. ST. JAMES HOSPITAL FOR MENTAL AND NERVOUS DISEASE. GROUP 49. SOUTH WEST METROPOLITAN REGION.

JUNIOR HOSPITAL MEDICAL OFFICER. The Hospital is approved as a Psychiatric Teaching Hospital and the post offers excellent experience in the treatment of the neuroses, the psycho-neuroses, the maladjusted child, and the problems of delinquency. The Neurological Department of the Hospital is also recognised by the examining bodies and arrangements are made to enable junior medical staff to fulfil the D.P.M. regulations regarding mental deficiency. Intending candidates may visit the Hospital by appointment.

JUNIOR HOSPITAL MEDICAL OFFICER (Locum Tenens) required for a period of approximately 6 months commencing 1st November, 1956.

Applications for either appointment, stating age, experience, qualifications, and the names and addresses of 2 referees, should be sent to the Physician-Superintendent within 14 days of the appearance of this advertisement.

READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER in the Area Department of Diseases of the Chest, for duty in the Reading Chest Clinic. The post offers wide experience in both tuberculous and non-tuberculous chest diseases and duties will include attendance at Prospect Park Hospital, Reading, and Peppard Chest Hospital, Henley. Facilities are available for postgraduate studies. Salary within the scale £775–£1075 p.a.

Applications, stating age and qualifications, together with names of 3 referees, should be sent to the Group Secretary, 3, Craven-road, Reading.

READING AREA HOSPITALS. Applications are invited for the post of SENIOR HOUSE OFFICER (pathology). Previous experience in pathology desirable, but not essential. Salary £745, less £150 board-residence.

Apply, stating age, qualifications with dates, nationality, present post, together with the names of 3 referees, to Group Secretary, 3, Craven-road, Reading.

READING. BATTLE HOSPITAL. (391 Beds.) Applications are invited from registered medical practitioners for the post of RESIDENT JUNIOR HOUSE SURGEON in the Area Accident and Orthopædic Department. Post vacant 1st October next. F.R.C.S. recognised. Also casualty duties. Salary £425–£525 p.a., less £125 board-residence.

Apply, stating age, qualifications with dates, nationality, present post, with 1 copy of recent testimonial, to Hospital Secretary.

REDHILL COUNTY HOSPITAL, Earlswood Common, REDHILL, SURREY. Locum ANÆSTHETIC REGISTRAR required for indefinite period from 1st October pending filling of vacancy for 2-year appointment. Married quarters available. Salary £17 10s. per week.

Apply Group Secretary, Redhill Hospital Management Committee, Earlswood Mount, Pendleton-road, Redhill (Redhill 3581, Ext. 20).

REDHILL. EAST SURREY HOSPITAL, Shrewsbury-road, REDHILL. RESIDENT HOUSE SURGEON (pre-registration appointment), vacant late September.

Apply Hospital Secretary, naming 2 referees.

ROCHDALE AND DISTRICT HOSPITAL MANAGE-MENT COMMITTEE. BIRCH HILL HOSPITAL. SENIOR HOUSE OFFICER (obstetrics and gynæcology) required mid-September. The post is for 12 months in the first instance and is recognised for the D.Obst.R.C.O.G.

Apply at once to the Group Secretary, Central Offices, Birch Hill Hospital, Rochdale.

ROCHFORD, ESSEX. GENERAL HOSPITAL. Locum GERIATRIC REGISTRAR required from 1st to 14th October, 1956.

Applications, stating age, &c., to the undersigned as soon as possible. J. C. FIELD, Secretary.

ROMFORD, ESSEX. VICTORIA HOSPITAL. (99 Beds.) RESIDENT HOUSE PHYSICIAN (Male) required immediately. Post not approved for pre-registration purposes.

Applications should be forwarded to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital Romford.

SKIPTON (near). GRASSINGTON HOSPITAL. (208 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER required for the above Hospital, which provides treatment for tuberculosis patients, men and women. Accommodation available for single applicants. Post tenable from 1st September, 1956.

Applications to Medical Superintendent.

SHREWSBURY. ROYAL SALOP INFIRMARY. (216 Beds.) HOUSE PHYSICIAN (pre-registration or otherwise), vacant 1st November, 1956.

Applications, with copy testimonials, to Group Secretary Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. CROSS HOUSES HOSPITAL. (34 maternity beds.) OBSTETRIC HOUSE SURGEON (pre-registration post), vacant immediately.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SALISBURY GROUP HOSPITAL MANAGEMENT COMMITTEE. REGIONAL PLASTIC AND ORAL SURGERY CENTRE, ODSTOCK HOSPITAL, SALISBURY, WILTS. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the post of SURGICAL REGISTRAR. Candidates should have had wide surgical experience and the possession of a higher surgical degree will be an advantage. Post vacant 16th November, 1956.

Application forms may be obtained from, and must be returned to, the Group Secretary, Odstock Hospital, Salisbury.

SCARBOROUGH HOSPITAL. (General—190 Beds.) Applications are invited for the post of NON-RESIDENT CASUALTY OFFICER (Junior Hospital Medical Officer) to commence duty approximately 1st November, 1956. Terms and conditions of service in accordance with those prescribed for medical and dental staffs. A furnished cottage is available for the successful applicant in the grounds of Cross Lane Hospital (1 mile distant), for which the present rent is £7 19s. 9d. per month.

Applications, giving age, qualifications, details of present and previous appointments, and the names of 2 referees, should be forwarded to the Hospital Secretary.

SHEFFIELD. CITY GENERAL HOSPITAL. Department OF PATHOLOGY GROUP LABORATORY. Applications are invited for the appointment of SENIOR HOUSE OFFICER (clinical pathology). Resident accommodation is available and optional. Opportunities for training in morbid anatomy, biochemistry, hematology and bacteriology. The work of this and the associated hospitals offers excellent experience to graduates who wish to make pathology their permanent career. The post is recognised for the D.Path.

Apply, giving details of age, qualifications, present and previous appointments with dates, and the names of 2 persons to whom reference may be made, to the Group Secretary at Nether Edge Hospital, Sheffield, 11.

SHEFFIELD. CITY GENERAL HOSPITAL. Sheffield REGIONAL HOSPITAL BOARD. Whole-time RESIDENT or NON-RESIDENT REGISTRAR (anæsthetics) required at the above Hospital. Recognised for the F.F.A.R.C.S. examination. Post vacant 25th November, 1956. Successful candidate to reside in hospital when "on call." This is a large general hospital (652 Beds) with a Department of Thoracic Surgery, a Regional Cardiological Centre and a Professorial Gynæcological Unit. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 1st October, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD. CITY GENERAL HOSPITAL. (Recognised for M.R.C.O.G.) Applications are invited for the resident post of SENIOR HOUSE OFFICER (gynæcology), vacant 1st January, 1957. Duties divided between units in charge of Professor of Obstetrics and Gynæcology, University of Sheffield, and full-time Consultant respectively.

Apply, giving full details of age, nationality, qualifications, present and previous appointments with dates, and the names of 2 persons for reference, to the Group Secretary, Nether Edge Hospital, Sheffield, 11, not later than 20th October.

SHEFFIELD REGIONAL HOSPITAL BOARD. Victoria HOSPITAL, MANSFIELD (302 Beds), KINGS MILL HOSPITAL, SUTTON-IN-ASHFIELD (172 Beds). (Recognised jointly for D.Obst. R.C.O.G.) Whole-time RESIDENT REGISTRAR (obstetrics and gynæcology) required. Married accommodation available at Victoria Hospital. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 1st October, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT or NON-RESIDENT SENIOR SURGICAL REGISTRAR (transitional appointment) required at City General Hospital, Sheffield, for 1 year in first instance. The successful candidate to reside at the Hospital when "on call." Applications invited from Senior Surgical Registrars in their fourth or subsequent years and from those who held such posts for 3 years or more but vacated them after 1st January, 1951.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 1st October, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. CHILDREN'S HOSPITAL. Applications are invited from registered medical practitioners for the resident post of HOUSE PHYSICIAN to the Professorial Unit at the above Hospital, vacant on 1st November, 1956 (6 months).

Applications, stating age, qualifications and experience with the names of 3 referees, should reach the Superintendent, The Children's Hospital, Western Bank, Sheffield, not later than 26th September, 1956.

SCOTLAND. EASTERN REGIONAL HOSPITAL BOARD. Radiodiagnosis. DUNDEE TEACHING HOSPITALS. Applications are invited for an appointment as SENIOR REGISTRAR in Radiodiagnosis at Dundee Royal Infirmary (510 Beds), and Maryfield Hospital, Dundee (370 Beds), both general teaching hospitals associated with the University of St. Andrews. Possession of the Diploma in Radiology is essential. A new Radiodiagnostic Department at Dundee Royal Infirmary has recently been brought into operation. Salary and conditions of service in accordance with national agreement.

Forms of application and further particulars from the Secretary to the Board, 430, Blackness-road, Dundee, with whom applications must be lodged not later than 29th September, 1956.

SCOTLAND. NORTHERN REGIONAL HOSPITAL BOARD. Applications are invited for the whole-time post of SENIOR REGISTRAR in Dermatology (limited amount of V.D. work involved). The post is non-resident and the main duties are at the Royal Northern Infirmary and Raigmore Hospital, Inverness. Previous experience in Dermatology is essential.

Forms of application and further particulars of the post are obtainable from the undersigned, to whom applications should be submitted by 8th October, 1956.

A. M. FRASER, M.D.,
Secretary and Administrative Medical Officer.
Office of the Northern Regional Hospital Board,
Raigmore, Inverness.

SCOTLAND. NORTHERN REGIONAL HOSPITAL BOARD. Applications are invited for the whole-time post of SENIOR REGISTRAR in General Surgery at the Inverness Group of Hospitals. Main duties are at the Royal Northern Infirmary, Inverness.

Schedules of application and further particulars may be obtained from the undersigned, with whom applications should be lodged by 15th October, 1956.

A. M. FRASER, M.D.,
Secretary and Administrative Medical Officer.
Office of the Northern Regional Hospital Board,
Raigmore, Inverness.

SCOTLAND. NORTHERN REGIONAL HOSPITAL BOARD. Applications are invited for the whole-time post of JUNIOR HOSPITAL MEDICAL OFFICER at the Ross Memorial Hospital, Dingwall. Applicants should have previous experience in obstetrics in hospital or general practice. The post is resident and a suitable house is available.

Schedules of application and further particulars may be obtained from the undersigned, with whom applications should be lodged by 15th October, 1956.

A. M. FRASER, M.D.,
Secretary and Administrative Medical Officer.
Office of the Northern Regional Hospital Board,
Raigmore, Inverness.

SCOTLAND. SOUTH-EASTERN REGIONAL HOS-PITAL BOARD. Applications are invited for the appointment of REGISTRAR to the Royal Edinburgh Hospital for Mental and Nervous Disorders, to work in the Professorial Unit in the Jordanburn Nerve Hospital. This appointment is made under the joint training scheme of the South-Eastern Regional Hospital Board and the Department of Psychological Medicine of the University of Edinburgh and the holder may be required to work in other centres in the region. Single accommodation available.

Applications, giving particulars of age, qualifications and previous experience, together with the names of 2 referees, should be sent to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 20th October.

SCOTLAND. SOUTH-EASTERN REGIONAL HOS-PITAL BOARD. Applications are invited for the appointment of REGISTRAR in Obstetrics and Gynæcology in the Professorial Unit at the Royal Infirmary of Edinburgh and the Simpson Memorial Maternity Pavilion, vacant on 1st January, 1957.

Applications, giving particulars of age, qualifications and previous experience, together with the names of 2 referees, should be submitted to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 20th October.

SCOTLAND. SOUTH-EASTERN REGIONAL HOS-PITAL BOARD. Applications are invited for the appointment of REGISTRAR in E.N.T. Surgery at the Royal Infirmary of Edinburgh, vacant on 15th December, 1956.

Applications, giving particulars of age, qualifications and previous experience, together with the names of 2 referees, should be submitted to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 20th October.

SCOTLAND. SOUTH-EASTERN REGIONAL HOS-PITAL BOARD. Applications are invited for the appointment of a REGISTRAR at Stratheden Hospital, Cupar, Fife. During the tenure of the post opportunities for interchange of duty and training at other centres in the Region may be available under joint training scheme of the South-Eastern Regional Hospital Board and the Department of Psychological Medicine of the University of Edinburgh. Residence is available.

Applications, giving particulars of age, qualifications and previous experience, together with the names of 2 referees, should be sent to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 20th October, 1956.

SOUTH CHESHIRE HOSPITAL MANAGEMENT COM-MITTEE. CREWE AND DISTRICT MEMORIAL HOSPITAL. (108 Beds and Annexe 34 Beds—Acute.)

Locum REGISTRAR (surgical) required at the above Hospital (approved for F.R.C.S.) for the month of October.

Applications, with full details, immediately, to the Group Secretary, Barony Hospital, Nantwich, Cheshire.

JUNIOR HOSPITAL MEDICAL OFFICER (anæsthetics), 3 years appointment. D.A. preferred. New operating suite to be opened shortly. Duties chiefly at general hospital and a Maternity Unit at another hospital. Hospital approved for D.A. Salary and conditions as per regulations.

Applications, giving age, details of experience, and names of 3 referees, immediately to Group Secretary, Barony Hospital, Nantwich, Cheshire.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (274 Beds.) 2 RESIDENT HOUSE PHYSICIANS required mid and end October. Pre-registration candidates eligible.

Applications, with copies of testimonials, should be forwarded to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton, as soon as possible.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL (278 Beds.) ORTHOPÆDIC HOUSE SURGEON required. Post recognised for Pre-registration Service and tenable for 6 months. The Hospital is the centre to which all trauma from a large industrial town and port is directed thus providing excellent experience in the treatment of traumatic conditions; patients with orthopædic conditions are also drawn from a wide area.

Applications, with copies of testimonials, should be sent as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL (274 Beds) and SOUTHAMPTON GENERAL HOSPITAL (472 Beds). SENIOR HOUSE OFFICER (E.N.T.) required beginning of October. This post is recognised for the F.R.C.S. (Eng.) and D.L.O. examinations and provides experience in all branches of E.N.T. work. The Group includes a diagnostic and distributing Hearing Aid Centre.

Applications, with copies of recent testimonials, should be forwarded as soon as possible, to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Orthopædic Surgery to fill a vacancy in the approved trainee establishment in the Brighton and Lewes Group of hospitals. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 6th October, 1956.

ST. ALBANS (near), HERTFORDSHIRE. Napsbury MENTAL HOSPITAL. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. JUNIOR HOSPITAL MEDICAL OFFICER (full-time), required. 3 years tenure. Some experience in psychiatry desirable. Single accommodation available.

Apply to Medical Superintendent by 2nd October, 1956.

STAFFORD HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (anæsthetics), Male or Female, resident. Recognised for D.A.

Applications to Group Secretary, Stafford Hospital Management Committee, 13, Foregate-street, Stafford.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. (854 Beds.) HOUSE OFFICER (general surgery), vacant now. Pre-registration post. Hospital recognised for F.R.C.S.

Detailed applications with copy testimonials to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. (845 Beds—100 maternity, 40 gynæcological.) SENIOR HOUSE OFFICER or HOUSE OFFICER (obstetrics and gynæcology), required. Post vacant early November. Recognised M.R.C.O.G. and D.Obst.R.C.O.G.

Applications to Hospital Management Committee Secretary, Stoke-on-Trent Hospital Management Committee, Princes-road, Stoke-on-Trent, as soon as possible.

SUTTON. BELMONT HOSPITAL. South West Metropolitan REGIONAL HOSPITAL BOARD. Applications are invited for appointment as PSYCHIATRIC REGISTRAR at above Hospital, which is principally concerned with the treatment of neuroses and the early psychoses. There are ample opportunities for research and the Hospital, which is recognised for the D.P.M., takes an active part in teaching in association with teaching hospitals. Candidates may visit the Hospital by appointment with the Physician-Superintendent.

Application forms may be obtained from the Group Secretary, Group Office, Belmont Hospital, Brighton-road, Sutton, Surrey, and completed forms (5 copies) should be returned to him within 2 weeks of the appearance of this advertisement.

SWANSEA HOSPITAL, Swansea. (403 Beds.) Glantawe HOSPITAL MANAGEMENT COMMITTEE. Registered medical practitioners are invited to apply for the resident appointment of SENIOR HOUSE OFFICER in the Gynæcological Department of the above Hospital. Vacancy 1st November, 1956.

Applications, stating age, and experience, together with copies of 2 recent testimonials, should be addressed to the Hospital Secretary.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. RESIDENT MEDICAL REGISTRAR required November.

Application forms from, and returnable to, Secretary, Windsor Group Hospital Management Committee, Alma-road, Windsor, by 30th September.

TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE. 2 SENIOR HOUSE OFFICERS (anæsthetics) required for the Tees-side Group of hospitals, 1 post vacant now and 1 vacant 15th October. The Group is recognised for the F.F.A.R.C.S. and D.A. Facilities are available for postgraduate study and emergency work is by rota.

Applications, with copies of 3 testimonials, to—

Dr. J. G. WARNOCK.

North Ormesby Hospital, Middlesbrough.

TUNBRIDGE WELLS (near). PEMBURY HOSPITAL, PEMBURY. (387 Beds.) Applications invited for post of RESIDENT ANÆSTHETIST (Senior House Officer), vacant 1st November. Post tenable for 12 months in the first instance and recognised for the D.A. and F.F.A.R.C.S. National Health Service salary, less £150 p.a. for residence.

Apply, stating age, qualifications and experience, together with 3 testimonials, to the Group Secretary, Tunbridge Wells Group Hospital Management Committee, Sherwood Park, Pembury-road, Tunbridge Wells.

TYNEMOUTH VICTORIA JUBILEE INFIRMARY. (115 Beds.) HOUSE SURGEON required at above Infirmary. Senior House Officer or House Officer grade according to experience. Post recognised for pre-registration purposes.

Applications, with names of 2 referees, to Group Secretary, Preston Hospital, North Shields.

WAKEFIELD. STANLEY ROYD HOSPITAL. Applications invited for post of JUNIOR HOSPITAL MEDICAL OFFICER in Psychiatry. Salary scale £775–£50–£1075. Married accommodation may be available.

Address written applications, giving full personal particulars, details of training, experience, &c., together with 2 names and addresses for reference, to W. BOWRING, Group Secretary, Victoria Chambers, Wood-street, Wakefield.

AMENDED

WALLINGFORD (near), BERKSHIRE. FAIR MILE HOSPITAL. BERKSHIRE MENTAL HOSPITALS MANAGEMENT COMMITTEE. Applications are invited for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER at above Mental Hospital of 1053 Beds. The post provides an excellent opportunity for postgraduate training in psychiatry, including outpatient clinic work and every facility is provided for study for the D.P.M. Suitable accommodation for a married man is available. The appointment is subject to the terms and conditions of service for hospital medical staff, the salary being £775–£50–£1075 p.a.

Applications, including details of age, qualifications and experience, together with the names of 2 referees, should be forwarded to the Medical Superintendent, Fair Mile Hospital, near Wallingford, Berks, within 10 days of the appearance of this advertisement.

WARRINGTON GENERAL HOSPITAL. (344 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (paediatrics), Male or Female, which will become vacant on 1st December, 1956. Post recognised for D.C.H. Scale of salary £745 p.a., less £150 for residential emoluments.

Applications to be forwarded to—

H. L. BOOT, Group Secretary,
Warrington and District Hospital Management Committee.
c/o General Hospital, Warrington, Lancs.

WELSH REGIONAL HOSPITAL BOARD.

REGISTRAR (obstetrics and gynæcology), St. Asaph General and Maternity Hospital (201 Beds). Post recognised for M.R.C.O.G. examination. Self-contained flat available. Post vacant immediately.

REGISTRAR (E.N.T. surgery), based Caernarvon and Anglesey General Hospital, Bangor, with visits to Llandudno General and other hospitals in area. Non-resident.

REGISTRAR in Infectious Diseases. Based City Isolation Hospital, Cardiff (219 Beds). To serve Cardiff Hospital Management Committee. Resident/non-resident.

Subject to review end of first year.

Application forms from Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 14 days.

WIGAN. ROYAL ALBERT EDWARD INFIRMARY. (200 Beds.) SENIOR HOUSE OFFICER in Orthopædic Surgery. Post vacant 1st November.

Applications to Secretary.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL. (313 Beds.) HOUSE OFFICER (anæsthetics). Post vacant 10th November. The Hospital is recognised for the F.F.A.R.C.S. and D.A.

Applications, with copies of 2 testimonials, to the Group Secretary.

WINDSOR. KING EDWARD VII HOSPITAL. Obstetric AND GYNÆCOLOGICAL HOUSE SURGEON required, Male or Female, for post vacant 1st October. Post recognised for M.R.C.O.G. and D.Obst.R.C.O.G. Not a pre-registration post. Successful candidate will be resident, at the Old Windsor Unit of this Hospital. Applicants required to be members of a Medical Protection Society.

Applications, stating age, nationality, qualifications, with dates, with copies of recent testimonials or names of 3 referees, to Hospital Secretary, as soon as possible.

WOLVERHAMPTON AND MIDLAND COUNTIES EYE INFIRMARY. SENIOR HOUSE OFFICER required for October. 100 Beds and busy Outpatient Department. Recognised for F.R.C.S. and D.O.M.S. examinations.

Applications to Secretary, Eye Infirmary, Compton-road, Wolverhampton.

Public Appointments

BIRMINGHAM. CITY OF BIRMINGHAM EDUCATION COMMITTEE. Applications are invited from registered medical practitioners (Men or Women) for appointment as SCHOOL MEDICAL OFFICER in the School Health Service. The possession of a D.P.H. or D.C.H. will be an advantage. Salary in accordance with Whitley Council scale of £1050–£50–£1200–£55–£1475 p.a. Appointment is subject to the appropriate superannuation act and to the passing of a medical examination.

Forms of application obtainable from the undersigned (stamped addressed envelope) must be returned not later than 6th October, 1956. Canvassing disqualifies.

E. L. RUSSELL, Chief Education Officer.
School Health Service, Queen's College Chambers,
38A, Paradise-street, Birmingham, 1.

KENT EDUCATION COMMITTEE require Assistant COUNTY MEDICAL OFFICER for North East Kent area. Salary in the scale £1050–£50–£1200–£55–£1475. Post superannuable. Duties mainly in School Health and Child Welfare Services. Experience in classification of educationally subnormal children an advantage.

Applications, stating age, qualifications, experience, and names of 2 persons to whom reference may be made as to professional ability and character, to Principal School Medical Officer, County Hall, Maidstone, by 4th October, 1956.

CHESHIRE COUNTY COUNCIL. Applications are invited from registered medical practitioners for appointment as SENIOR ASSISTANT MEDICAL OFFICER on the County Medical Staff. The work will be concerned mainly with children under 5 years of age, and will include assistance in supervising child-welfare centres and the work of the health visitors. A knowledge of mental ill-health and its prevention in young children will be an advantage. The appointment is superannuable and subject to medical examination. The salary scale will be that applicable to Assistant Medical Officers, plus £125 at all stages—i.e., £1175–£50–£1325–£55–£1600. Previous experience will be taken into consideration, and car and subsistence allowance will be paid according to the County Scale.

Forms of application may be obtained from the undersigned, to whom they should be returned by 20th October, 1956.

ARNOLD BROWN, County Medical Officer.

24, Nicholas-street, Chester.

DUBLIN. LOCAL APPOINTMENTS COMMISSION. Positions vacant. COUNTY MEDICAL OFFICERS (*a*) co. Mayo, (*b*) co. Donegal. Salary scale in each case: £1623–£1847.

Application forms and particulars from the Secretary, Local Appointments Commission, 45, Upper O'Connell-street, Dublin. Latest time for receiving completed application forms 5 P.M. on 5th October, 1956.

GOVERNMENT OF BAHAMAS. Applications invited from Doctors with qualifications registrable in the United Kingdom for following vacancies:—

(*a*) ASSISTANT MEDICAL OFFICER for duty at Princess Margaret Hospital or elsewhere as required by the Chief Medical Officer.

(*b*) DISTRICT MEDICAL OFFICER for duties in a specified area.

Appointments on permanent basis with pension (non-contributory) or on agreement for 3 years in first instance. Salary £1400 a year. No income-tax. Unfurnished quarters or rent assistance. Free passages on appointment for Officer, wife, and up to 2 children and, if appointed on agreement, free passages back to United Kingdom on completion of engagement.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting No. BCD. 117/27/02).

SOUTHERN GAS BOARD. Applications are invited for the new and pensionable post of Whole-time ASSISTANT MEDICAL OFFICER. Previous experience in industrial medicine would be an advantage. The salary will be on Senior Staff scale, Grade D, £1375–£1575, or Grade E, £1525–£1725, or by arrangement with the successful applicant. The successful candidate will be required to pass a medical examination and, unless already subject to a Pension Scheme by virtue of the Gas (Pension Rights) Regulations, 1950, will be required to join the Board's Staff Pension Scheme.

All applications must be made on a form which may be obtained from the Personnel Manager, Southern Gas Board, 164, Above Bar, Southampton, and completed forms should be returned by Monday, 22nd October, 1956.

P. VALON BENNETT, Personnel Manager.

STAFFORDSHIRE COUNTY COUNCIL. Biddulph URBAN DISTRICT COUNCIL; LEEK URBAN DISTRICT COUNCIL. Applications are invited for the separate part-time appointments of ASSISTANT COUNTY MEDICAL OFFICER AND SCHOOL MEDICAL OFFICER, MEDICAL OFFICER OF HEALTH of the Biddulph Urban District and MEDICAL OFFICER OF HEALTH of the Leek Urban District. The appointments together will constitute whole-time, the allocations being 5 half-days, 3 half-days and 3 half-days, respectively. The proportionate salary for each appointment is calculated in accordance with the latest agreed scale, and increments will be given for previous service in the same capacity, the ranges being:—

County Council—
£596 11s. 10d.–£28 8s. 2d. (3)–£31 5s. 0d. (5)–£838 1s. 4d.
Biddulph Urban District Council—
£501 16s. 4d.–£15 (4)–£561 16s. 4d.
Leek Urban District Council—
£501 16s. 4d.–£15 (4)–£561 16s. 4d.

A car is necessary and an allowance will be paid.

The posts are superannuable, and the successful candidate must pass a medical examination and produce his birth certificate. Applicants must be fully qualified medical practitioners with experience in public health duties, and must hold the Diploma of Public Health or its equivalent. The candidate appointed will, as regards the County Council duties, act under the direction of the County Medical Officer of Health, and will be required to perform such duties as may from time to time be prescribed. As regards the duties of Medical Officer of Health, he will be subject to the Sanitary Officers (Outside London) Regulations, 1935 and 1951, and to the sole control and direction of the Urban District Councils. The County Council appointment will be subject to 3 calendar months notice in writing on either side.

Forms of application may be obtained from the County Medical Officer of Health, County Buildings, Stafford, and should be returned to him not later than by first post on 2nd October, 1956.

T. H. EVANS, Clerk of the County Council.
R. W. TRACE, Clerk of the Biddulph U.D.C.
S. F. ESLAND, Clerk of the Leek U.D.C.

County Buildings, Stafford, 10th September, 1956.

WEST BROMWICH. COUNTY BOROUGH OF WEST BROMWICH. Applications invited from registered medical practitioners for appointment of DEPUTY MEDICAL OFFICER OF HEALTH AND DEPUTY PRINCIPAL SCHOOL MEDICAL OFFICER. Salary scale £1307, by 4 increments of £55 and 1 of £50 to £1577. The Council have adopted conditions of service agreed by the Medical Council of the Whitley Councils for Health Services.

Further particulars and form of application from the undersigned. Closing date for applications 1st October, 1956.

Town Hall, West Bromwich. J. M. DAY, Town Clerk.

NORFOLK COUNTY COUNCIL. Applications are invited from registered medical practitioners holding the Diploma in Public Health for appointment as SENIOR ASSISTANT MEDICAL OFFICER on headquarters staff. In addition to administrative work, the duties will include the medical examination of staff and deputising for other medical officers. The salary scale (subject to Council approval) will be £1343 10s.–£52 10s.–£1606. Travelling and subsistence allowances will also be paid.

Application forms, together with further particulars of the post, can be obtained from the County Medical Officer, 29, Thorpe-road, Norwich, to whom completed applications should be sent not later than 8th October, 1956.

WESTMINSTER CITY COUNCIL AND HOLBORN BOROUGH COUNCIL. Joint appointment of PRINCIPAL ASSISTANT MEDICAL OFFICER OF HEALTH (permanent superannuable post). Salary £1515–£55–£1680 p.a. Applicants to be registered medical practitioners and to hold a registered Public Health qualification; age not to exceed 45 years. The person appointed will act as Principal Assistant Medical Officer of Health for the 2 Boroughs. His services will be allocated in the proportion of three-fourths to Westminster and one-fourth to Holborn.

Further particulars from and applications (marked "Principal Assistant Medical Officer of Health") stating age, war service, qualifications, present and past appointments, with copies of 3 recent testimonials, to the Town Clerk, Westminster City Hall, Charing Cross-road, W.C.2, by 12th October, 1956.

THE REPUBLIC OF THE SUDAN. The Ministry of Health invite applications for the post of SURGICAL SPECIALIST. Candidates must possess the necessary professional qualifications—viz., F.R.C.S. or its internationally recognised equivalent. Age between 28 and 48. Salary range £E1750–£E2330 (for Junior Specialists) or a flat £E2330 for Specialists. Candidates for this post may apply for secondment from the National Health Service for a period of up to 3 years under the terms of the circular letter No. REB/(52)106EG(52)101 of 30th September, 1952. The appointment will be on a short-term contract for a period up to 5 years. Starting salary will be determined according to age and qualifications. A bonus of 1 months salary for each completed year of satisfactory service will be payable and an outfit allowance of £E50 on signature of contract.

Further particulars and application form can be had on application to Dr. E. P. PRATT, 137, Harley-street, London, W.1.

General Practice

For an Executive Council post (England and Wales) apply on form E.C.16A *obtainable from the council. Mark envelope "Vacancy."*

PORT MORESBY (PAPUA AND NEW GUINEA). LOCUM required for 6 months from mid-October with possibility of taking over practice, which includes some midwifery. £150 (ster.ing) tax-free, and all found, plus half air fare. Interview in London.—Apply with brief particulars: Address, No. 244, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Hospital Services: Non-Medical Appointments

ARCHWAY GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from Technicians (Associate I.M.L.T. or equivalent), with experience in Clinical Biochemistry for a post now vacant in the Biochemical Laboratory of the Department of Endocrinology, New End Hospital. Salary according to Whitley scale.

Detailed applications, naming 2 referees, to Group Secretary, 46, Cholmeley-park, N.6, within 10 days.

GLASGOW, N.1. STOBHILL GENERAL HOSPITAL. Applications are invited from suitably qualified candidates for the post of BIOCHEMIST (Senior grade) at the above Hospital. The applicant appointed will work under the direction of a Consultant Clinical Biochemist (Medical) from whom further information may be obtained. Salary, &c., in accordance with Whitley Council scale (rising to maximum of £1230 p.a.).

Applications, together with the names and addresses of 2 referees, should be sent to Medical Superintendent not later than 3 weeks after the appearance of this notice.

Miscellaneous

Chief Medical Officer required by British Mining Company operating in Burma. Salary and allowances £2365 p.a., plus free living accommodation, domestic help, and accident insurance. Travelling expenses of wife and children paid by the Company. Contract for 38½ months, with 2½ months leave on full pay every 18 months.—Applications, stating age, qualifications, and experience to Box L.690, c/o 191, Gresham House, E.C.2.

Cheshire: close to Birkenhead and Liverpool. Easily managed Nursing-home registered for 22. 15 rooms, 3 bathrooms, usual offices. Garden. Price freehold £6000 as a going concern. Mortgage available. Would consider letting.—Further details from JACKSON-STOPS & STAFF, 25, Nicholas-street, Chester (Tel.: 21522/3).

Required, medical translators Russian-English. Also translators from other languages.—Please address full details regarding qualifications and fees to: Address, No. 246, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimen of urine and £1 1s. fee. Hæmatology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

Applicants for posts requiring testimonials copied or duplicated should communicate with MANTON SECRETARIAL SERVICE LTD., 98, Victoria-street, S.W.1 (Phone: VICtoria 0141), who are specialists in this kind of work.

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Indications: Nasal congestion, chronic and allergic rhinitis, and sinusitis.

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